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CONTENTS

PAGE

Occupational Lung Cancer: A Review. RICHARD DOLL 181

Biochemical Studies on the Toxicity of Tetraethyl Lead and Other Organo-lead Compounds. JILL E. CREMER 191

Dermatitis in the South Wales Mining Industry: A Report of a Survey of Two Collieries. BRYAN F. MATTHEWS 200

Accidents in a Naval Dockyard. C. P. COLLINS 208

The Acute Toxic Effects of Black Smoke. R. E. PATTLE, G. D. WEDD, and F. BURGESS 216

Some Hazards in the Manufacture and Use of Plastics. D. KENWIN HARRIS 221

Patterns of Sickness Absence in a Railway Population. CECIL GORDON, A. R. EMERSON, and DEREK S. PUGH 230

The Action Exerted by Certain Pneumoconiotic Factors upon the Acid Mucopolysaccharide Contents of Pulmonary Macrophages. N. GH. LUPU, DOINA VELICAN, C. VELICAN, and V. OLINESCU 244

Miscellanea:

A Case of Cirrhosis and Primary Carcinoma of the Liver in Chronic Industrial Arsenical Intoxication. S. S. JHAVERI 248

Book Reviews 250

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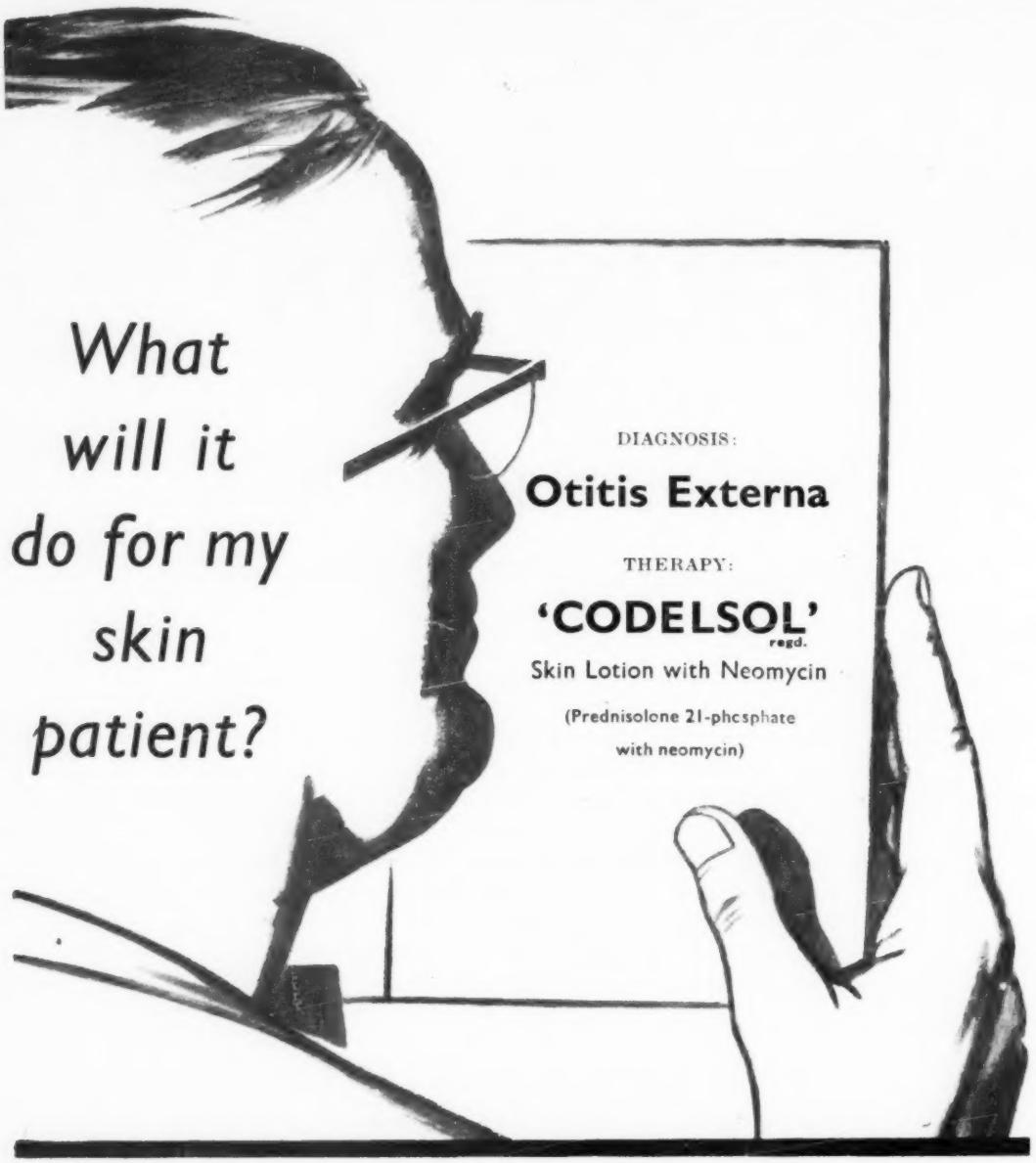

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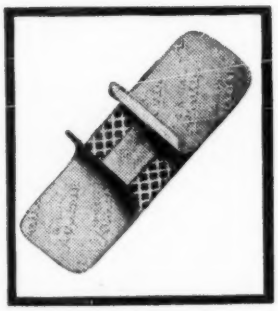

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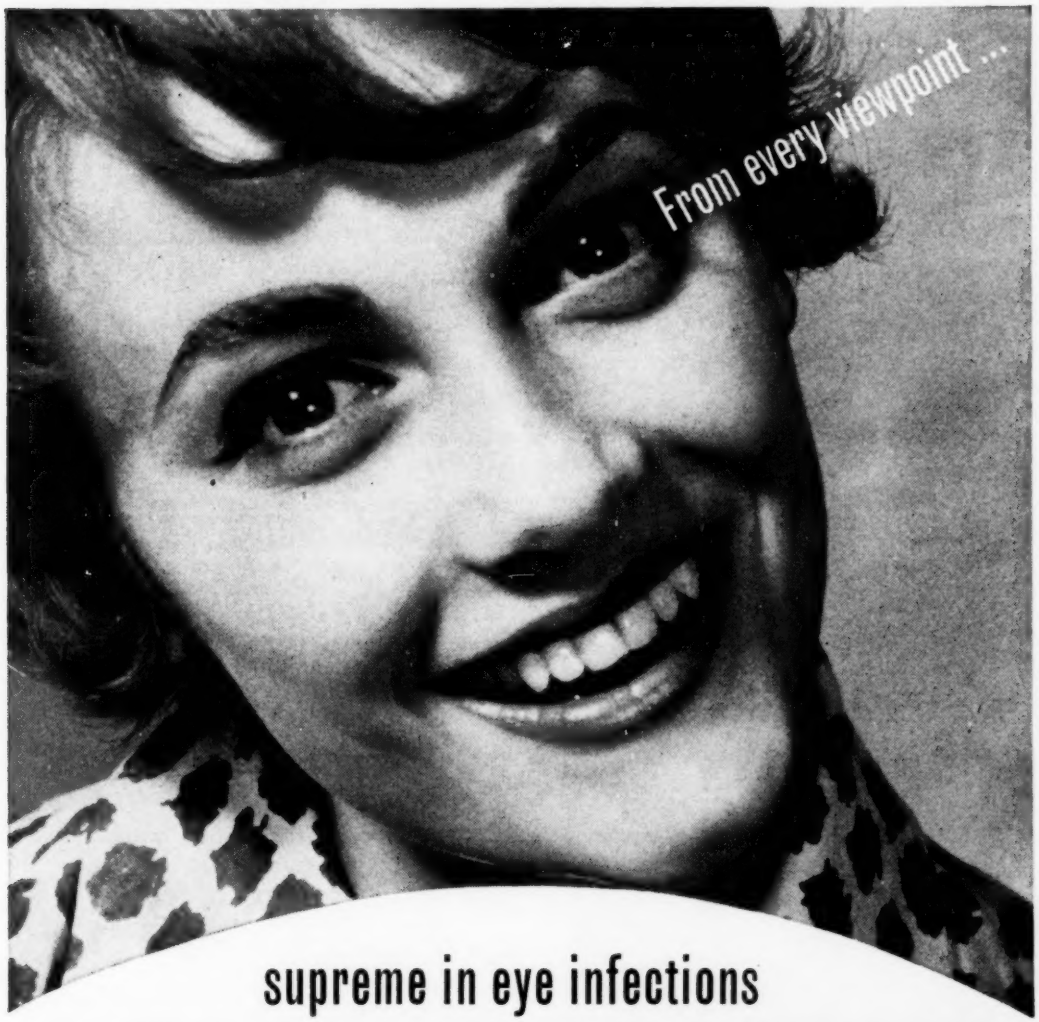

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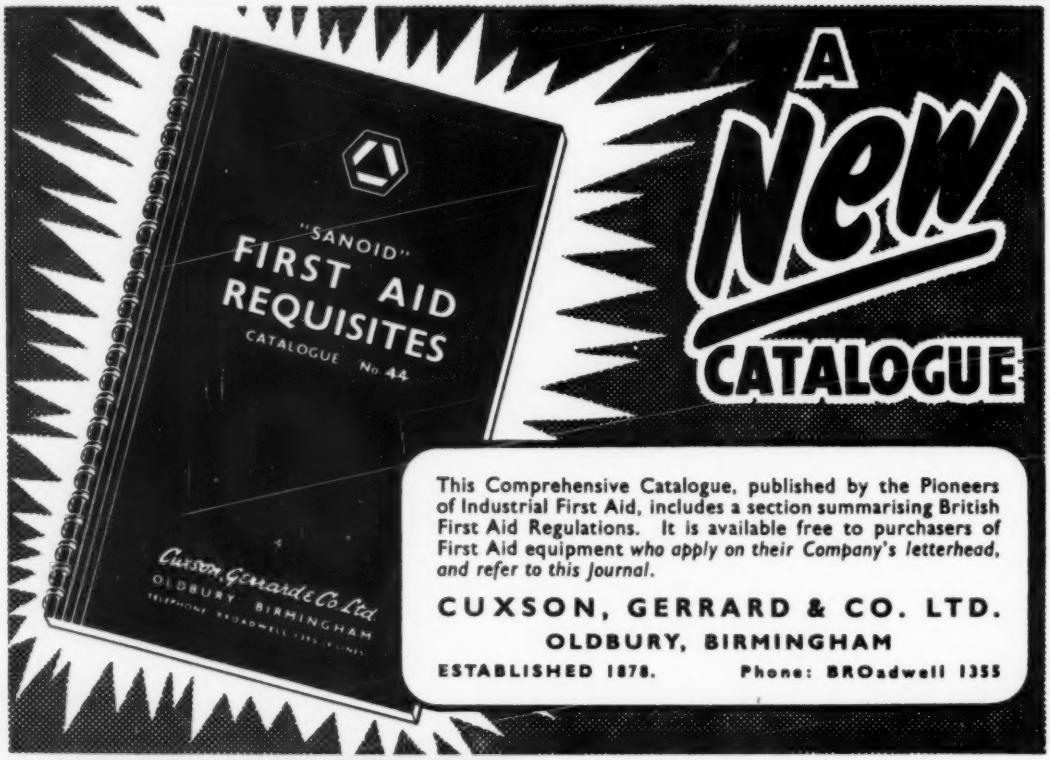
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OCCUPATIONAL LUNG CANCER: A REVIEW

BY

RICHARD DOLL

From the Statistical Research Unit, Medical Research Council

(RECEIVED FOR PUBLICATION FEBRUARY 4, 1959)

Study of occupational factors was the method which led to the discovery of the first pure carcinogen. The study of such factors among patients with lung cancer has already been extremely fruitful and has led to the discovery of at least five, and possibly more, independent industrial risks. The carcinogenic factors concerned have not all been determined with certainty, but several of them appear to be simple inorganic compounds. The study of occupational factors also provides knowledge, difficult to obtain in any other way, of the biological relationship between exposure to carcinogens and the development of cancer in man and it is reasonable to hope that it will, in the future, make an important contribution to our knowledge of the fundamental mechanisms of carcinogenesis.

Established Risks

Radioactivity.—The first risk to be recognized was that run by the miners of Schneeberg and Jachymov. This is not of direct interest to us in Britain but it is of considerable indirect interest, as it provides one of the few sources of evidence from which we can assess the possible significance of the effect of exposure to ionizing radiations. The miners of Schneeberg and Jachymov had been known to suffer from a specific pulmonary disease for 500 years, but it was not until 1879 that the disease was recognized to be cancer. It is impossible now to be certain of the exact extent of the risk, but it is probable that 90% of the tumours causing death among the miners were bronchial in origin and that somewhere between 40% and 75% of all men who were continuously employed in the mines died of the disease. The best estimate of the risk is that approximately 1% of the miners were affected annually; this would mean that the risk must have been about 10 times greater than the large risk to which the general population of Great Britain is now exposed. Full data may be found in the reviews by Lorenz (1944) and Šikl (1950).

The mines have been worked successively for silver, nickel, cobalt, bismuth, arsenic, radium, and uranium. The characteristic which most sharply distinguished them from other mines was the high radioactivity of the ore and it may be noted that these mines provided the ore from which, in 1898, the Curies isolated radium. The first time a suggestion that the disease might be due to radioactivity appeared in the medical literature was in 1921 when Margarete Uhlig, herself a native of Schneeberg, commented that she had seen the suggestion "in an article by a layman". An average value for the concentration of radon in the air of the mines was found to be 3×10^{-9} curies per litre (Evans and Goodman, 1940), but the measurements were made at a time when the ventilation had been improved and the previous values may have been substantially higher.

The dose of radiation received by the lungs would have been due more to the short-lived daughter products of radon carried on ore dust particles than to the radon itself, and the nature and amount of the atmospheric dust would have been of great significance in determining the quantity of radioactive substances inhaled and the site of their deposition. Bale and Shapiro (1955) calculated that with normal dusty air a concentration of 3×10^{-9} curies of radon per litre would result in the tracheal epithelium receiving an average dose of about 0·2 rad per day. Owing to selective deposition the local dose might be more than 10 times the average, so that the miners who died of the disease may have received local doses of 10,000 rad of α-rays (Glucksmann, Lamerton, and Mayneord, 1957).

Experiments have shown that true squamous tumours can be produced in the bronchi of rats by radioactive cerium and by plutonium (Lisco and Finkel, 1949; Lisco, personal communication) and similar tumours have been elicited by bead implants of radioactive strontium, by single intratracheal injections of radioactive cerium, and by repeated injections of radioactive sulphur (Cember, 1958). The dose received locally in the lungs of the Schneeberg miners is calculated to have been of the same order as that received in the vicinity of the bone sarcomas which developed in the girls who ingested

radium and there is no reason to doubt that radioactivity was the cause of the lesion. It may, however, have been assisted by other factors. In animal experiments, cancer has been induced by radiation more easily when non-specific inflammation was also present (Burrows and Clarkson, 1943) and silicosis was rife among the miners. Silicosis was, however, not particularly severe in those lungs in which cancer also developed.

No other groups of workers have been shown to have suffered a high incidence of bronchial tumours as a result of exposure to high doses of radioactivity. Many cases are believed to have occurred among the workers at the Shinkolobwe mines in the Belgian Congo, but no data have been published. At Port Radium in Canada, the miners have been highly mobile and no epidemiological evidence is available. Some evidence may eventually be obtained about the miners of the Colorado Plateau. Several of the mines in this part of the U.S.A. have had atmospheric radioactivity comparable to that at Schneeberg (Holaday, 1955), and an attempt is now being made to trace the effect on the workers. At most other uranium mines the ores have been of much lower grade and the existence of a risk would be difficult to detect. Whether exposure to the smaller doses of radioactivity in the normal environment is likely to produce any cases of the disease is unknown. If the incidence of cancer is proportional to the dose of radiation received it must be supposed that some few cases are likely to be due to this cause. The Londoner is exposed to about one ten-thousandth of the radioactivity that was present in the air of the Schneeberg mines and it would, therefore, appear that less than 1% of cases could be due to radioactivity. It may be, however, that small doses of this order are entirely free from risk and that no cases at all are produced. In the present state of knowledge it is impossible to give a tolerance level for radon with confidence: the official level is 10^{-11} curies per litre, but the only sensible attitude to take is that if workers have to be exposed to levels of radioactivity above those normally occurring, these levels should be kept to the minimum possible.

Nickel.—The only form of occupational lung cancer to have been prescribed as an occupational disease in Great Britain is that which occurs among men exposed to nickel powder formed "by decomposition of a gaseous nickel compound". It is, therefore, regarded as an occupational disease among the men employed at a large refinery in South Wales, where the nickel carbonyl process of refining is used. The first cases were reported by Amor (1939); since then many other cases have been reported and it is now known that at least 131 cases of lung cancer and 62 cases of nasal cancer have occurred among the men employed at this particular refinery in the last 35 years (Doll, 1958; Morgan, 1958). Cancer of the nasal cavities is normally such a rare disease that the occurrence of so many cases in the period is convincing evidence of the existence of a specific industrial hazard. It is, however, a different matter with regard to cancer of the lung. This disease has become so common that it is necessary to make a detailed assessment of the number of cases to be expected in the absence of a special hazard, before it can be concluded that the observed number is excessive.

Hill (1939) obtained data for the numbers and age distribution of the men employed by the Company, or on the Company's books as pensioners, for the years 1931 and 1937. Little change occurred between these years and he concluded that the average population for the two years provided a reasonable estimate of the population at risk for the period 1929-35. During this period, 16 deaths were attributed to cancer of the lung and 11 to cancer of the nose, whereas he estimated that the number expected from the experience of all England and Wales would have been 1 and between 0 and 1 respectively. In contrast, the numbers of deaths from other forms of cancer and from other causes were close to the expected numbers. Division of the men into two broad categories, depending on whether or not they were employed on any of the specific processes, showed that the whole excess was concentrated on the process workers, although these constituted little more than half the total number of employees. Doll (1958) has studied the data for a later period by an indirect method. From the records of the local medical officers of health he found that 48 out of 200 deaths reported among nickel workers during the period 1948-56 were attributed to cancer of the lung, *i.e.*, 24·0%, and a further 13 were attributed to cancer of the nose, 6·5%. It was estimated that even in this period the risk of dying of lung cancer was nearly five times the high non-industrial risk and that the risk of nasal cancer was 150 times the "normal" risk. These values were calculated for all grades of workers; for men described as process workers they were higher. But although the mortality among the workers remains high it seems probable that the hazard in the industry has now been greatly reduced, if not eliminated. According to Morgan (1958), four deaths from lung cancer would have been expected to occur among men who started employment at the works after 1924; only six have occurred, and, perhaps more significantly, none of the post-1924 workers has developed cancer of the nose.

Despite the sudden change in the extent of the hazard, it is not possible to define the carcinogen with certainty. From Morgan's data, it is clear that the men who ran the greatest risk were engaged in calcining the original matter or in the extraction of the calcine with sulphuric acid. In contrast, relatively few cases occurred among the men who were principally employed in the sheds where the nickel was volatilized and decomposed. Five cases of lung cancer have, moreover, now been reported from a small Norwegian nickel refinery using an electrolytic process (Løken, 1950; Goldblatt and Goldblatt, 1956) and there is no reason to believe that the risk is confined to the use of the nickel-carbonyl process. The only obvious change which took place in the period 1920-24 was the substitution of an almost arsenic-free sulphuric acid for an acid containing large amounts of arsenic and Morgan has, therefore, suggested that arsenic may have been the responsible factor. This is not very likely, however, as even large amounts of arsenic in the atmosphere of another factory have not produced the same high risk of lung cancer and they have produced no cases of cancer of the nose (see subsequent section). Large quantities of dust used to be produced in the early stages of the process and it seems most likely that the agent was present in the original raw material, which contained nickel and copper in almost equal amounts. Nickel, in powdered form, has been shown to be capable of producing sarcoma in rats by both intrafemoral and subcutaneous injection (Hueper, 1955) and it has also produced adenomatoid changes in the lungs of rats and guinea-pigs when the animals were exposed to it in the atmosphere for prolonged periods (Hueper, 1958a).

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radium and there is no reason to doubt that radioactivity was the cause of the lesion. It may, however, have been assisted by other factors. In animal experiments, cancer has been induced by radiation more easily when non-specific inflammation was also present (Burrows and Clarkson, 1943) and silicosis was rife among the miners. Silicosis was, however, not particularly severe in those lungs in which cancer also developed.

No other groups of workers have been shown to have suffered a high incidence of bronchial tumours as a result of exposure to high doses of radioactivity. Many cases are believed to have occurred among the workers at the Shinkolobwe mines in the Belgian Congo, but no data have been published. At Port Radium in Canada, the miners have been highly mobile and no epidemiological evidence is available. Some evidence may eventually be obtained about the miners of the Colorado Plateau. Several of the mines in this part of the U.S.A. have had atmospheric radioactivity comparable to that at Schneeberg (Holaday, 1955), and an attempt is now being made to trace the effect on the workers. At most other uranium mines the ores have been of much lower grade and the existence of a risk would be difficult to detect. Whether exposure to the smaller doses of radioactivity in the normal environment is likely to produce any cases of the disease is unknown. If the incidence of cancer is proportional to the dose of radiation received it must be supposed that some few cases are likely to be due to this cause. The Londoner is exposed to about one ten-thousandth of the radioactivity that was present in the air of the Schneeberg mines and it would, therefore, appear that less than 1% of cases could be due to radioactivity. It may be, however, that small doses of this order are entirely free from risk and that no cases at all are produced. In the present state of knowledge it is impossible to give a tolerance level for radon with confidence: the official level is 10^{-11} curies per litre, but the only sensible attitude to take is that if workers have to be exposed to levels of radioactivity above those normally occurring, these levels should be kept to the minimum possible.

Nickel.—The only form of occupational lung cancer to have been prescribed as an occupational disease in Great Britain is that which occurs among men exposed to nickel powder formed "by decomposition of a gaseous nickel compound". It is, therefore, regarded as an occupational disease among the men employed at a large refinery in South Wales, where the nickel carbonyl process of refining is used. The first cases were reported by Amor (1939); since then many other cases have been reported and it is now known that at least 131 cases of lung cancer and 62 cases of nasal cancer have occurred among the men employed at this particular refinery in the last 35 years (Doll, 1958; Morgan, 1958). Cancer of the nasal cavities is normally such a rare disease that the occurrence of so many cases in the period is convincing evidence of the existence of a specific industrial hazard. It is, however, a different matter with regard to cancer of the lung. This disease has become so common that it is necessary to make a detailed assessment of the number of cases to be expected in the absence of a special hazard, before it can be concluded that the observed number is excessive.

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Asbestos.—The first case of cancer of the lung in association with asbestosis was reported by Lynch and Smith (1935) in the U.S.A. Since then about 80 to 100 cases have been reported from Britain, Canada, Germany, and the U.S.A.—the greatest number from Britain. Some authors are impressed by the paucity of the numbers more than by their frequency (Bohlig and Jacob, 1958; Braun and Truan, 1958) but many cases have not been reported. The first indication that the association was not coincidental was obtained by Merewether (1949), who found that lung cancer was reported at necropsy more frequently among asbestotics than among silicotics and this was confirmed by Gloyne (1951) who, in a personal series, found lung cancer in 14·1% of persons dying with asbestosis (17 out of 121), against 6·9% among persons dying with silicosis (55 out of 786). Since the prevalence was higher in men (19·6% among the male asbestotics in Gloyne's series) and since the proportion of men is likely to have been lower among asbestotics than silicotics, the contrast between subjects of the same sex would probably have been greater than that reported for both sexes together. The data have been criticized on the grounds that the material was selected and was not representative of all persons exposed respectively to asbestos and silica dust. There is, however, no reason to suppose that the criteria by which cases were referred to Gloyne differed in respect of the two types of pneumoconiosis.

Only two direct studies of the mortality among men exposed to asbestos have so far been reported. Braun and Truan (1958) observed the mortality among 5,958 Canadian asbestos miners over a six-year period and found nine deaths "proved" to be due to lung cancer and three in which the diagnosis was "suspected". They concluded that if the mortality had been similar to that recorded for the whole Province there would have been eight lung cancer deaths and they concluded that "the asbestos miners in the Province of Quebec do not have a significantly higher death rate from lung cancer than do comparable segments of the general population". In contrast, Doll (1955) found a very high lung cancer mortality among 113 men who had been employed for 20 or more years in parts of a British asbestos factory where they were likely to have been exposed to asbestos dust. The men were followed from the time of completing their 20 years' service until the end of 1954, that is, for an average of just over nine years. In this period there were altogether 39 deaths, including 11 attributed to lung cancer; the numbers of deaths expected from the age-specific national morbidity rates were respectively 15 and one. The incidence of lung cancer was found to be highest among the men who had had the longest exposure to the conditions existing before the 1931 "Asbestos Regulations" were made effective and it decreased progressively as the duration of such exposure was reduced.

These two sets of observations are not necessarily contradictory. The explanation may, perhaps, be found in a difference between the environmental conditions. Neither the size not the chemical constitution of the dust particles are likely to have been the same (chrysotile in the first study and a mixture of chrysotile and hornblende in the second) and it may be noted that asbestosis was believed to be present in under half of the Canadian cases (five out of 12), whereas it was present in all the British cases. It seems reasonable to conclude that exposure to asbestos dust does give rise to lung cancer, but that the circumstances in which it will do so have not yet been fully defined.

The fibrils of asbestos consist of giant molecules of polymerized silico-oxygen tetrahedra arranged in chains or bands. In Canadian asbestos, the silica is present as hydrated magnesium silicate containing 6% of iron oxide; in other, industrially less important types, the silicates may be calcium and magnesium or sodium and iron. In Hueper's view (1957) the carcinogenic activity may result from the physical form of the material as a linear polymer and the mechanism may be similar to that by which cancer has been induced in animals with various polymerized carbon compounds. Alternative views are discussed by Goldblatt (1958). Animal experiments with asbestos itself have so far been negative.

Gas Production.—The combustion and distillation products of coal provide a rich source of carcinogens and they have long been recognized as capable of producing cancer of the skin among men who come into close contact with them in the course of their work. It would, therefore, not be surprising if the fumes and dust from coal tar were capable of giving rise to cancer of the lung. Evidence that this might be so has been obtained in three countries. In Japan, between 1931 and 1937, 21 cases of lung cancer were diagnosed among gas generator workers and ex-workers of the Yawata steel works and there can be no reasonable doubt that this indicates an abnormal incidence (Kuroda and Kawahata, 1936; Kuroda, 1937; Kawahata, 1938). Lung cancer was—and still is—a rare disease in Japan and no deaths were attributed to lung cancer among the other employees at the works during a period when 12 such deaths occurred among the gas workers. In contrast, the mortality from other types of cancer was of the same order among both groups of employees, that is, three deaths among approxi-

mately 500 gasworkers and 49 deaths among approximately 19,000 other workers. It follows that among the gasworkers lung cancer accounted for 80% of all the cancer deaths, *i.e.*, 12 out of 15. The men worked directly above the ovens and, when the coal was stirred, yellow-brown gas streamed directly over them.

In Canada, Sutherland (personal communication) found that the lung cancer mortality among men who worked in the retort house of one Canadian gasworks was 15 times greater than that recorded for the general population of the district; among these workers 19 deaths were attributed to cancer and the primary site was recorded as being in the respiratory system in nine, *i.e.*, in 47%. The retorts used were of the horizontal type and the men who operated them were exposed from time to time to quantities of hot fumes. Employees who had never been employed in the retort house showed no excess mortality from respiratory cancer and neither did the employees at another works, where the retorts had long been changed to a more modern type. In Britain, Kennaway and Kennaway (1936 and 1947) analysed the occupations of men certified as dying of lung cancer between 1921 and 1938. Four out of the five occupations with the highest mortality had special exposure to the fumes (labourers at "patent fuel" works, gas stokers and coke oven chargers, gas producer men and gas works foremen and inspectors). Among men employed in these occupations the expected number of deaths from lung cancer was 51 and the observed number was two and a half times as great, *i.e.*, 125. A slightly lower ratio was found some years later in a study of 2,071 male pensioners of a large London gas company (Doll, 1952). Twenty-five deaths were attributed to lung cancer and the expected number, at the rates recorded for all male Londoners of the same ages, was 14. The excess is small, but the investigation covered a multiplicity of occupations and the risk may have been substantially greater for those men who were directly concerned with the production process. Reid and Buck (1956), on the other hand, were unable to find any evidence of an increased risk among men employed in the production of metallurgical coke. With the passage of time and the increase in the mortality experienced by the non-industrial population, it becomes progressively more difficult to recognize a specific industrial hazard and it will require a detailed investigation over many years before it is possible to say whether or not there is any risk involved in the operation of the modern type of retort. Such an investigation has been started under the auspices of the Medical Research Council, but it may be several years before a decisive result is obtained.

Quantitative estimates of the amount of carcinogen likely to be inspired are not as yet available. Measurements at one works where vertical retorts were employed showed that the amount of 3:4-benzpyrene in the air might be five to 10 times more than in the general atmosphere of a large English town (Hughes and Somerville, personal communication). If it were possible to link this pollution with a particular incidence of the disease, it might be of great help in assessing the risk associated with "normal" urban smoke.

Suspected Risks

Arsenic.—That arsenic is capable of causing cancer in man is demonstrated by the occurrence of cancer of the skin among patients who had received arsenic by mouth and among men who were exposed to arsenical dust in the course of their work. The latter group are known also to be subject to ulceration of the nasal septum. It is, therefore, not surprising that arsenic has long been suspected to be a cause of cancer of the lung. Arsenic was present in small amounts in the ore of the Schneeberg and Jachymov mines and in the raw materials used by the nickel refiners of South Wales and in both instances it has, at times, been regarded as the effective carcinogen. In fact, the evidence to implicate arsenic is slight. Four cases of lung cancer among sheep dip workers were notified to the Ministry of Labour between 1939 and 1943 (Merewether, 1944) and one case occurred in a man who made a sodium arsenite insecticide and had a heavily pigmented skin, numerous warts, and a perforated nasal septum (Bridge, 1941).

The only direct evidence was obtained by Hill and Faning (1948), who analysed the cause of death among the employees of a small English factory in which arsenical powders were prepared from sodium arsenite. Examination of the death entries in the offices of the local registrars of deaths provided records of 75 deaths among male employees between 1910 and 1943. The causes of death were compared with the causes recorded for other male manual workers resident in the same area during the same period and it was found that the proportion attributable to cancer was higher for the factory workers (29·3%) than for the other workers (12·9%); moreover, it was higher still among the chemical workers who were most likely to come into direct contact with the arsenical dust (39·0%). The high proportion of cancer deaths was largely due to an excess of deaths from cancer in two sites. Out of 22 cancer deaths, three were attributed to cancer of the skin and seven were attributed to cancer of the respiratory system (lung five, mediastinum one, larynx one) against expected numbers estimated to be 0·1 and

1·0 respectively. Environmental studies, carried out at the same time, showed that very large amounts of arsenic might be present in the air, ranging—at mouth height in one part of the factory—from 310 μg. per m.^{3} to over 4,000 μg. with a mean of about 1,000 μg. (Perry, Bowler, Buckell, Druett, and Schilling, 1948). Large amounts of arsenic were found in the urine and hair of the workers and the majority of the chemical workers were grossly pigmented; approximately one-third had warts.

It seems probable, therefore, that exposure to inorganic arsenic in the air may produce lung cancer, if the amount present is sufficient to produce gross evidence of arsenicism. In the absence of such evidence, it seems most unlikely that the amount of arsenic inspired could be sufficient to account for any important industrial risk of the disease.

Iron.—The siderosis caused by pulmonary retention of Fe_2O_3 or $Fe_3O_4 \cdot H_2O$ is usually considered to be innocuous, but there is some evidence to suggest that it may lead to an increased risk of lung cancer—particularly when it is associated with silicosis. The most detailed data have been obtained by Faulds and Stewart (1956) in relation to haematite miners. Haematite consists principally of ferric oxide, but it also contains 10 to 12% of silica. It has been mined in Cumberland since Roman times, but the introduction of new drills, just before the first world war, greatly increased the dustiness of the work and effective measures for the suppression of dust were not taken for over 20 years. Faulds and Stewart found that among the miners (1) the prevalence of lung cancer at necropsy increased sharply from 4·4% in 1932-47 (four in 92 necropsies) to 14·6% in 1948-53 (13 in 89 necropsies); (2) the prevalence was greater than among other Cumberland males of approximately the same age distribution, *i.e.*, 9·4% (17 in 180 necropsies) against 2·0% (45 in 2,221 necropsies); and (3) at least six growths appeared to have arisen from sidero-silicotic masses. Such evidence is, however, not conclusive. The prevalence of lung cancer increased sharply throughout England during the same period and it is impossible to be sure that the incidence among the miners as a whole was really higher than normal. Necropsy data of this type are difficult to interpret, because subjects who come to necropsy may not be representative of the population from which they are drawn. Even in the period since 1948 only 56% of the miners who died came to necropsy. Compensation is payable if death is attributed to silicosis and those who came to necropsy must be presumed to include the great majority of the miners dying with pulmonary symptoms. The true incidence may, therefore, have been as low as 13 cases among 160 miners and this figure (8·1%) is not very different from that which would have been expected from the national mortality data. Among other Cumberland males, on the other hand, the reasons for which a necropsy is performed are presumably, different. The most important reason is likely to be sudden death, so that the proportion of necropsy cases coming, in which there is evidence of lung cancer, may be below the average for the population as a whole.

A moderately high mortality has been reported among several other groups of iron workers. Turner and Grace (1938) found that foundry workers, smiths, and metal grinders had a mortality from lung cancer higher than that for any other occupational group in Sheffield and metal grinders were also found to have suffered an excessive mortality from lung cancer in Kennaway and Kennaway's (1947) study of the deaths certified as being due to lung cancer in the whole of England and Wales. In the period 1921 to 1938 they found 39 deaths recorded among metal grinders, whereas they estimated that the expected number was 22·2. The ratio of the observed and expected number of deaths (1·76 to 1) was exceeded only by three groups of gas or pitch workers out of the 56 occupational groups examined. In the Registrar-General's study of occupational mortality for England and Wales in the period 1930-32, "metal moulders and casters" and "iron foundry furnacemen and labourers" occupied fourth and fifth places in the list of occupations with a high mortality from lung cancer; the standardized death rates were respectively 93% and 88% above average (Registrar-General, 1938). In the succeeding analysis for the period 1949-53, the iron and steel worker still showed an increased mortality, but the excess was less marked (Registrar-General, 1958); this, however, would be expected

TABLE 1

NATIONAL MORTALITY DATA FOR VARIOUS GROUPS OF FOUNDRY WORKERS, 1949-53*

Social Class	Occupation	No. of Deaths at Ages 20-64 Years	Standardized Mortality Ratio
	Moulders and core-makers		
IIIc	Iron or steel	158	155
IIIc	Non-ferrous	28	122
	Foundry furnacemen		
IVb	Iron or steel	17	142
IIIc	Non-ferrous	13	144
	Foundry labourers		
IVb	Iron or steel	136	131
IVb	Non-ferrous	12	80
IIIe	All skilled occupations, other than in mining, transport, or clerical work or the Armed Forces	13,038	99
IVb	All partly skilled occupations, other than in agriculture	4,452	99

*Extracted from data published by the Registrar-General (1958).

in view of the great increase in the general mortality from the disease. The data are summarized in Table 1. A similar excess has also been demonstrated in Scotland (Registrar-General for Scotland, 1956; Morrison, 1957).

Evidence of a different type has been obtained from the study of patients. In two large-scale studies in the U.S.A. Wynder and Graham (1951) and Breslow, Hoaglin, Rasmussen, and Abrams (1954) found that a higher proportion of men with lung cancer than of men with other diseases had been employed as "hot metal" workers—and the majority of these are likely to have worked with iron. A similar study in England, however, failed to confirm this finding (Doll and Hill, reported by Doll, 1953).

In sum, there is a considerable body of evidence to suggest that there is a specific industrial hazard from exposure to iron dust or fumes, with or without additional exposure to silica. None of it, however, is conclusive and at the present time the case must be regarded as not proven.

Possible Risks

Isopropyl Oil.—The only evidence to incriminate isopropyl oil comes from the U.S.A., where it was found that six among 75 men who were employed for more than five years on the manufacture of isopropyl oil died of respiratory cancer; four of these cancers arose in the nose, one in the larynx, and one in the lung (Weil, Smyth, and Nale, 1952). Nasal cancer is so rare that it is impossible to dismiss this finding as coincidence, but it remains to be seen whether there is a risk of any other respiratory cancer. In view of the association of lung and nasal cancer among the nickel workers, it would not be surprising if a lung cancer risk was also discovered.

Beryllium.—The possibility that men exposed to beryllium might develop lung cancer was first suggested in 1948 because of the appearance of sarcoid-like lesions in the lungs of beryllium workers and because bone tumours had been induced experimentally by the injection of beryllium into rabbits (Gardner and Heslington, 1946). Interest in the suggestion was enhanced when Vorwald (1955) found that it was possible to produce true bronchial carcinoma in rats by causing them to inhale beryllium. Only three cases of lung cancer have however, as yet been recorded among men who have been exposed to beryllium (Kahlau, 1954; Hardy, 1955), and it is quite possible that the association is coincidental. It is interesting to note that beryllium is the only non-radioactive substance with which it has as yet been possible to produce squamous cancer of the bronchi in animals.

Other Industries.—A high mortality from lung cancer has been recorded in certain areas of Montana, U.S.A., where the main industry is the mining and smelting of copper; the data are summarized in Table 2. The possibility that a carcinogenic substance occurs in association with copper ore is of particular interest in view of the fact that the nickel cancer risk in South Wales was apparently limited to the period when the nickel ore also contained large quantities of copper. It must be borne in mind, however, that many of the Montana mines are highly radioactive and radioactivity is also a possible explanation.

TABLE 2

LUNG CANCER MORTALITY IN FOUR COUNTIES OF MONTANA, U.S.A., 1947-48*

County	Major Industry	Number of Cases of Lung Cancer		Annual Death Rate from Lung Cancer per 100,000	
		M	F	M	F
Dear Lodge	Copper smelting	21	0	146	0
Silver Bow	Copper mining	27	2	49	4
Cascade	Coper mining and smelting	20	5	46	12
Gallatin	Agriculture	1	0	5	0

The crude death rate from lung cancer among white males in the U.S.A. in 1947 was 11 per 100,000.
*After Lull and Wallach, cited by Hueper (1956).

Ask-Upmark (1955) has suggested that there may be a risk from exposure to printing ink. He found an unexpectedly high proportion of printers among a small series of lung cancer patients in Sweden (eight out of 125) and demonstrated experimentally that printing ink was carcinogenic to the skin of mice.

Osburn (1957) has reported an unusual frequency of lung cancers among Africans in the Gwanda region of Southern Rhodesia and attributes this to a specific risk associated with the local mines. Between 1948 and 1956 22 cases of lung cancer was diagnosed among Africans; all were in men. Out of 36 cancers found at necropsy on African men, 14 arose in the bronchi, a very much higher proportion than has commonly been reported in Africa. Of the 22 men, 13 were employed in the mines when they were taken ill and six others are believed to have worked there at some time previously. One of the patients had worked at an asbestos mine, but the other mines at which the men had been employed were worked principally for gold; in some the ore contains a high proportion of arsenopyrite.

Industries of Interest because of Absence of Risk

Two groups of industries are of particular interest because the evidence suggests that there is no

substantial risk of lung cancer among their employees, although there are theoretical reasons for thinking that there might have been. The first of these includes all those industries in which the employees have a special exposure to the fumes of petrol or diesel-driven engines. These fumes may contain measurable quantities of 3:4-benzpyrene and other carcinogenic polycyclic hydrocarbons and it has been thought that they may contribute to the excess mortality from lung cancer among the residents of large towns. Kennaway and Kennaway (1947) selected a group of outdoor occupations and found that the mortality from lung cancer among them was slightly higher than average. Similar results were obtained for a later period by the Registrar General (1958). The data are summarized in Table 3.

TABLE 3

MORTALITY FROM LUNG CANCER IN ENGLAND AND WALES IN CERTAIN OCCUPATIONS SPECIALLY EXPOSED TO ROAD DUST AND VEHICLE FUMES

Occupation	Standardized Mortality Ratio		
	Kennaway and Kennaway (1947)		Registrar-General (1958)
	1921-32	1933-38	1949-53
Paviours, street masons, concretors, and asphalters	209	137	135
Council labourers, road sweepers, and dustmen	173	167	—
Drivers of horse-drawn vehicles	144	131	222
Motor drivers (goods and passengers)	142	153	118

In contrast, retrospective studies of the occupational histories of patients with lung cancer have provided no evidence of a disproportionate number of patients employed in this type of occupation (Wynder and Graham, 1951; Doll, 1953; Breslow *et al.*, 1954). The clearest evidence, however, comes from the experience of the London Transport Executive. In an analysis of the mortality amongst the various groups of employees, Raffle (1957) found (1) that the total mortality from lung cancer was somewhat lower than that for men of the same age in London generally, and (2) that the mortality among bus drivers and conductors and the engineering staff at bus garages was lower than that observed among underground railway workers and the engineering staff at trolley bus depots. These results suggest that the fumes of petrol-driven motors are unlikely to be a major cause of the disease; but they are not of great significance in relation to diesel engines, as these have not been on the road in large enough numbers long enough for diesel fumes to be expected to have produced any evidence of cancer—even if they were capable of doing so.

The second group of industries consists of those with a hazard of silicosis. Data collected by the Miners' Phthisis Medical Bureau (1936) in Witwatersrand showed that in over 3,000 necropsies on European miners the prevalence of lung cancer was the same, irrespective of the presence of silicosis; moreover it was practically the same as that found at the General Hospital, Johannesburg, among men who had never worked underground. In South Wales, James (1955) found that the prevalence of lung cancer at necropsy was, at each age, less among coal-miners than among non-miners from the same area and that the prevalence fell as the degree of pneumoconiosis increased. Some degree of pneumoconiosis is present in most forms of industrial lung cancer, but all investigators agree that there is no quantitative relationship between silicosis and the presence of the cancer. It must be concluded that where there is an industrial hazard of lung cancer it is due to some specific characteristic of the industry and not to a non-specific effect of pneumoconiosis.

Contribution of Industrial Studies to the Understanding of Carcinogenesis in General

Site Specificity.—In all the industries in which a specific risk of lung cancer has been recognized, the risk has been confined to the lungs or, at the most, to the lungs and to one other site. In one industry (the refining of nickel) there has also been an important risk of nasal cancer and it is possible that there may be a risk of nasal cancer associated with the chromate industry. A few cases have been recorded among chromate workers by Baetjer (1950) and this disease is normally so rare that the occurrence of even two or three cases is suggestive. In no industry is there any evidence to suggest that a risk of lung cancer is accompanied by a risk of laryngeal cancer. It is clear, therefore, that agents which are capable of producing cancer in the bronchi, and which presumably reach the bronchi via the upper respiratory passages, do not necessarily affect the mucosa of the upper parts of the respiratory tract; in fact, they generally do not. This may, perhaps, be explained by variation in the susceptibility of the tissues to the particular agents, but so little is known about the physical properties of the various dusts and gases involved that the true explanation may be much simpler and the differences may depend on quantitative differences in the amounts of the carcinogen deposited.

In two industries (the production of gas and the manufacture of certain arsenical compounds) there is also known to have been an increase in the incidence of cancer of the skin. In both these, there is a clear reason for the selection of this site: in the

gas industry the skin may be heavily contaminated with coal-tar and, in the case of exposure to arsenic, the skin serves as the organ of excretion. No other type of cancer is known to have increased in any of the industries which have been studied and it is reasonable to conclude that the production of lung cancer is the result of a local reaction rather than of a general metabolic disturbance.

Cramer's Hypothesis.—In 1934, Cramer suggested that the susceptibility to cancer might be determined by intrinsic (possibly genetic) factors and that the effect of environmental agents might be to determine the site at which the predestined cancer would eventually appear. The suggestion was put forward tentatively to account for the fact that the crude death rates from cancer were similar in the two sexes and in several different countries, while the distributions of the primary sites were grossly different. A more detailed examination of the mortality rates, taking into account the differences in the age distribution of the populations, makes this hypothesis less attractive than it originally appeared. Nevertheless, it has continued to influence medical thought and it is worth noting that the data obtained from industrial studies weigh heavily against it. If the hypothesis were true, it would be expected that an increased incidence of lung cancer among men in a particular occupation would be associated with a diminished incidence of cancer in other sites. The results of several studies demonstrate that this is, in fact, not so. Sufficiently detailed data are not available for the miners of Schneeberg and Jachymov, but in all the other industries in which a specific risk of lung cancer has been established, it has been shown that the mortality from other types of cancer has been undiminished (Hill, 1939; Machle and Gregorius, 1948; Doll, 1952, 1955, 1958; Bidstrup and Case, 1956).

Latent Period.—In all types of industrial cancer there has been a long interval between the year of first employment in the industry and the appearance of the cancer. Lung cancer is no exception. The latent period has been most commonly of the order of 15 to 30 years, but some few growths have appeared less than five years after first employment and others as long as 40 or 50 years afterwards. The occurrence of some of the growths with a very short latent period may be coincidental, but it is impossible to set precise limits to the possible durations which may be observed. Whether the risk of occurrence of an industrial cancer decreases after a certain length of exposure is uncertain. The reduction in the number of cases with the longer latent periods is a necessary result of the reduction in the number of men alive in the older age groups and the apparent reduction is often exaggerated by the failure to trace all the cases which occur among men who leave the industry. Cases are known to occur many years after all exposure has ceased, but there are as yet no data which would enable an estimate to be made of the reduction in risk which follows the cessation of exposure. It is, in fact, not yet known whether the removal of the hazard has any significant effect on the size of the risk once there has been a prolonged exposure. Knowledge of the relationships between risk and duration of exposure would be of great importance to the understanding of the mechanism of carcinogenesis. One of the most practical ways of obtaining this information would be by a detailed study of the risk among cohorts of employees who continue to be employed in a hazardous industry and among those who cease employment after various periods.

Variety of Carcinogens.—Animal experiments have shown that a great variety of substances are capable of carcinogenic activity. This knowledge has been reinforced by the finding that exposure to many different industrial substances is capable of producing cancer in man. In the case of lung cancer, the range is particularly wide—radioactive substances, polycyclic hydrocarbons, asbestos, and simple inorganic compounds of arsenic, chromium, and nickel (possibly even the elements themselves). The discovery of a large risk in relation to some of these simple substances is surprising and it may be expected that a more exact definition of the conditions under which they can cause cancer will lead to an important increase in our knowledge of the mechanism of carcinogenesis generally.

Conclusion

The history of industrial lung cancer has shown that a specific industrial hazard may be overlooked for many years by both management and employees. The first indication of a risk has usually been an acute medical observation that a disproportionate number of the patients presenting with lung cancer have been employed in a particular industry; alternatively evidence has been provided by the occupational mortality statistics for the whole country or by an analysis of the occupations recorded on the death certificates in the locality in which the industry was situated. Sometimes this evidence has been overwhelming, as in the case of the Schneeberg miners; but usually, to obtain proof of the existence of a risk, it has been necessary to carry out a detailed study of the fate of selected workers over a number of years and to compare the mortality among them with that recorded for other

populations. Lung cancer is a rapidly fatal disease and although it is now a common cause of death, its prevalence is so low that, even in the presence of a major risk, the examination of as many as 1,000 workers may fail to reveal any cases at all on a single occasion.

In recent years the mortality from lung cancer due to non-industrial causes has increased enormously; now in Britain lung cancer accounts for more than 10% of all deaths among men aged from 45 to 64 years, the ages at which a risk of industrial cancer may most readily be detected. In these circumstances, the discovery of a new risk by simple clinical observation is difficult and if any additional risks remain to be discovered it is probable that they will be revealed by planned prospective studies, undertaken with the special object of finding out whether any risks exist. That all the existing risks have been discovered seems most unlikely. Moreover, new materials and new processes are being introduced into industry almost daily and there is no reason to suppose that they will necessarily all be free from risk. It may be expected that industrial studies will continue, as in the past, to make important advances in our knowledge of all aspects of carcinogenesis. In this respect, detailed studies of the relationship between exposure, incidence, and duration of latent period may be of particular value.

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BIOCHEMICAL STUDIES ON THE TOXICITY OF TETRAETHYL LEAD AND OTHER ORGANO-LEAD COMPOUNDS

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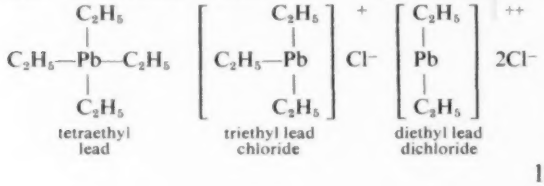
The actions of purified tetra-, tri-, and di-ethyl lead on rats and rat brain slices and brain brei have been examined. A method based on a reaction with dithizone and capable of estimating tri- and di-ethyl tin in rat tissues has been developed.

After injection into rats tetraethyl lead is converted into triethyl lead and this is responsible for the toxic effects. Diethyl lead is much less toxic and the effects are different. The utilization of lactate and the oxidation of glucose by brain brei and slices respectively are inhibited by triethyl lead. A similar effect is seen in slices taken from rats poisoned with tetra- or tri-ethyl lead. Rat liver cell microsomes readily convert tetraethyl to triethyl lead and the latter is stable and remains in the animal tissues for several days. The concentration of triethyl lead in the brain is not high in comparison with other tissues but brain tissue appears to be unduly sensitive to its toxic action.

Neither tetra- nor tri-ethyl lead reacts with B.A.L. or ethylene-diamine-tetra-acetic acid (E.D.T.A.). Diethyl lead reacts with B.A.L. but not with E.D.T.A.

Tetraethyl lead has been added to petroleum as an anti-knock agent for many years and is known to be toxic to man. Casualties have usually occurred among persons cleaning out petrol tanks, and a very full account has been given by Cassells and Dodds (1946). The signs of poisoning indicate that the main site of action is the central nervous system; in severe cases tremors and convulsions develop, often leading to death. Similar signs can be produced by giving tetraethyl lead to laboratory animals.

In tetraethyl lead all valencies are satisfied. It is insoluble in water but soluble in ethanol and fat solvents. On exposure to intense daylight it decomposes and triethyl lead and diethyl lead can be detected as decomposition products. The ionic forms of the chloride salts of triethyl lead and diethyl lead are depicted below since they were used throughout the study to be described. Both are water soluble and ionize to give a mono-valent and di-valent ion respectively. None of these organo-lead compounds chelate with ethylene-diamine-tetra-acetic acid (E.D.T.A.), whereas lead acetate chelates most readily.



Although it was suggested by Buck and Kumro (1930) and by Machle (1935) that the toxic action of tetraethyl lead might be due to its more water-soluble decomposition products rather than to the parent compound itself, there are no published data to support this idea. There is no information on the biochemical action of organo-lead compounds.

This paper describes some biochemical effects of tetra-, tri-, and di-ethyl lead and lead acetate on rat brain metabolism. A method has been developed for estimating tri- and di-ethyl lead as intact organo-lead ions in biological material and the presence of a system in rat liver capable of converting tetraethyl lead to triethyl lead has been shown.

Methods

Male adult albino rats of 175 to 230 g. body weight maintained on M.R.C. diet No. 41B (Bruce and Parkes, 1956) were used.

Slices of brain cortex and liver were prepared using a Stadie-Riggs type slicer (Stadie and Riggs, 1944).

For studies on the metabolic activity of brain cortex slices, each Warburg flask contained 3 ml. of Krebs-Ringer phosphate solution (Umbreit, Burris, and Stauffer, 1951), with 0·011 M glucose, tissue slice of 50 to 60 mg. wet weight, and 0·2 ml. of 20% (w/v) KOH in the centre

well for absorption of CO_2. The manometers were placed in a water bath at 37°C., gassed for 5 min. with 100% O_2, equilibrated for a further 10 min., and O_2 uptake was measured at intervals up to 75 min. QO_2 was calculated as μl. of O_2/mg. dry weight of tissue/hr. The control QO_2 value was 13·26 ± 1·14 (S.D.). Lactic acid was estimated by the technique of Barker and Summerson (1941) and pyruvic acid by the method of Friedemann and Haugen (1943).

Rat Brain Brei.—The suspensions were prepared in ice-cold 0·1 M phosphate buffer *p*H 7·4 as previously described (Aldridge and Cremer, 1955).

Fractionation of Liver Homogenates.—This process was carried out essentially by the centrifugation techniques of Schneider (1948). A 10% (w/v) liver homogenate was prepared in 0·3 M ice-cold sucrose. The nuclei and cellular debris were separated off by centrifuging at 600 g. for 10 min. at 0°C. The mitochondria were sedimented at 7,500 g. for 20 min. The supernatant containing the microsomes and soluble cell material was separated into microsomes and clear supernatant by centrifuging at 105,000 g. for 60 min at 0°C. using a "spinco ultra" centrifuge.

Purification of Organo-lead Compounds.—Tetraethyl lead, triethyl lead chloride, and diethyl lead dichloride were supplied by Dr. Boyd. These compounds are unstable even when stored in subdued light and require purification before use. Tetraethyl lead was separated from traces of triethyl lead and diethyl lead by washing an ether solution with conductivity water three to four times in subdued light and allowing the ether to evaporate. The purified sample was stored in the dark at −20°C. A stock ethanolic solution of 40 mg. tetraethyl lead/ml. was prepared and stored in a blackened, stoppered tube at 0°C. A fresh stock solution was prepared every four weeks. Triethyl lead chloride was purified by recrystallization from a large volume of ether in subdued light. Aqueous stock solutions of 10 mg./ml. were prepared every two weeks and were also stored in blackened, stoppered tubes at 0°C. On storage of diethyl lead dichloride for several weeks triethyl lead could be detected together with water-insoluble material. It was purified by washing twice with ether to remove triethyl lead followed by recrystallization of diethyl lead dichloride from an ethanolic extract in subdued light. Fresh aqueous solutions were prepared just before each experiment.

Injections of Lead Compounds in Rats.—Tetraethyl lead was given by intravenous (tail vein) injection as solution in ethanol. Each rat received not more than 0·1 ml.; triethyl lead chloride and diethyl lead dichloride were given by intraperitoneal injections as solutions in 0·9% NaCl. Lead acetate was given by intravenous injection as an aqueous solution. Each rat received not more than 0·2 ml. of a solution 100 mg./ml.

Tissue Water Content of Brain and Spinal Cord.—The water content was taken as the difference between the wet weight and the dry weight after heating at 104°C. Values in Table 9 are expressed as % water in the original wet weight.

Estimation of Organo-lead Compounds.—The procedures used were based on the dithizone method for the estimation of triethyl tin in biological material described by Cremer (1957). For the estimation of triethyl lead, tissue samples of between 0·4 and 1·0 g. wet weight were homogenized in 5ml. water using a "nelco" homogenizer. Water (15 ml.) was added to the homogenate and the protein was precipitated with perchloric acid (30% v/v; 5 ml.). The contents were mixed thoroughly and centrifuged for 10 min. A 20 ml. sample of the supernatant was taken, neutralized with 5N NaOH (approximately 5·5 ml.) and 2 ml. of borate-E.D.T.A. buffer was added (19 g. of $Na_2B_4O_7$, 10 H_2O; 12 g. of boric acid; 4 g. E.D.T.A. diluted to 1 litre).

The following procedures were carried out in a darkened room owing to the instability of the coloured complex to be formed. Chloroform (10 ml.) was added followed by 1 ml. of dithizone reagent 0·04% (w/v) dithiocarbazone in $CHCl_3$ and the contents mixed thoroughly for 2 min. using a mushroom-ended glass rod. The aqueous layer was removed by suction. The chloroform layer, containing the triethyl lead-dithizone complex, was read against a dithizone control in 2 cm. cells at a wavelength of 610 mμ using a "unicam" SP.600 spectrophotometer. Two drops of acetic acid (Analar) were then added to each tube (triethyl lead does not complex with dithizone under acid conditions) and readings taken again. The difference value of the two readings, giving the amount of dithizone used, was compared with the amount used by a standard concentration of triethyl lead. Recovery of triethyl lead added to 1 g. wet weight samples of tissue was between 70 and 80%. The values given in Tables 2, 3, and 9 for the amount of triethyl lead in the various tissues have been corrected for this recovery.

Tetraethyl lead does not form a coloured complex with dithizone. When triethyl lead was estimated in the presence of tetraethyl lead, owing to the instability of the latter compound in an acid medium, the protein was precipitated by adding $Ba(OH)_2$ (0·3N; 5 ml.) and $ZnSO_4$ [5·35% (w/v) $ZnSO_4 \cdot 7H_2O$; 5 ml.] to the tissue homogenate in 15 ml. water. After centrifuging, a 20 ml. sample of the supernatant was taken and 2·0 ml. of borate-E.D.T.A. buffer was added. The procedure was then exactly as described above.

Using the procedures described above recoveries of diethyl lead from tissues except blood were low, and the results obtained are of qualitative value only. From blood 90% diethyl lead was recovered.

Results

Action of Lead Compounds in Rats.—Although there have been reports of experimental organo-lead poisoning (Harnack, 1878; Mason, 1921; Bischoff, Maxwell, Evans, and Nuzum, 1928; Buck and Kumro, 1930; Kehoe and Thamann, 1931; Mortensen, 1942; and Morelli and Preziosi, 1953) few comparisons of different organo-lead compounds in the same species have been made. Therefore, the four lead compounds, tetra-, tri-, and di-ethyl lead, and lead acetate, were given to rats and the main symptoms observed are recorded in Table 1. The routes of administration were as described under Methods.

TABLE 1

ACTION OF LEAD COMPOUNDS IN RATS *IN VIVO*

Compound	Dose (mg./kg. body weight)	Route	Number of Rats	Symptoms			Death
				Excitable	Tremors	Convulsions	
Tetraethyl lead	20	Intravenous	4	+ + + +	+ + + +	+ +	4
	15·4	,,	4	+ + + +			0
Triethyl lead	15	Intraperitoneal	4	+ + + +	+ + + +	+ + + +	4
	11·2	,,	4	+ + + +	+ +		2
Diethyl lead	40	Intraperitoneal	2	Slight loss of weight			0
	20	,,	2				0
Lead acetate	100	Intravenous	4	Loss of weight			0

TABLE 2

ACTIVITY OF BRAIN SLICES FROM RATS GIVEN LEAD COMPOUNDS

Compound	Dose (mg./kg.)	Time after Injection (hr.)	Brain Slices (% of Control)			Tri-ethyl Lead Found (μg./g. wet wt.)			
			$Q O_2$	Lactic Acid	Pyruvic Acid	Blood	Liver	Kidney	Brain
Tetraethyl lead	20	4	50	295	46	76	45	23	2·4
	20	24	33	280	36	62	29	25	19·0
	10	4	80	150	88	12	15·5	10	—
	10	24	60	235	71·5	12	20	10	—
Triethyl lead chloride	10	4	54·5	330	58·5	65	39	24	4
	10	24	53	300	52	35	30	19	8
						Diethyl lead			
Diethyl lead dichloride	40	4	91	120	100	—	—	—	—
	40	24	80	200	80	68	—	—	—
	20	24	107	100	100	25	—	—	—
Lead acetate	100	4	100	116	126				
	100	24	100	155	125				

*These values are from different animals.

After receiving either tetra- or tri-ethyl lead the signs of poisoning which developed were identical. With lethal doses of either compound the rats became quiet and uneasy immediately after injection. Sometimes they gasped during the first half-hour. Twenty-four hours later the rats behaved very excitably, especially in their reactions to sudden noise and movement in the proximity of their cage. They remained in an excitable state and during the following 24 hours they developed in addition severe continuous tremors generalized throughout the body. This stage was often accompanied by violent, intermittent convulsions leading to death. After the highest doses given (tetraethyl lead 26 mg./kg. body weight and triethyl lead chloride 33 mg./kg.) death never occurred in less than 24 hours and after tetraethyl lead deaths might not take place for up to 14 days. Rats given just sublethal doses also became very excitable and developed a continuous tremor of the lower jaw only. Sometimes pairs of rats were observed to be standing facing each other as if sparring. Similar behaviour was reported by Stoner, Barnes, and Duff (1955) in rats given trimethyl tin acetate. The only difference observed between tetra- and tri-ethyl lead in their action on rats was the dose required to produce identical symptoms. The LD50 value was 11·2 (9·6 to 13·6) mg./kg. body weight for triethyl lead chloride and 15·4 (13·2 to 18·0) mg./kg. for tetraethyl lead calculated by the method of Weil (1952).

Rats given diethyl lead dichloride intraperitoneally in doses of 20 and 40 mg./kg., apart from initial uneasiness and loss of appetite during the first few days, did not behave differently from the controls over a 12-week observation period. Similar results were found in rats given lead acetate intravenously in a dose of 100 mg./kg., although the initial loss in body weight was more pronounced. Four 200 g. male rats lost an average of 30 g. each during the first four days but steadily gained weight from the second week onwards.

Distribution of Organo-lead Compounds in Rats.—In the Methods section a procedure is described for the estimation of triethyl lead, as the complete organic lead ion, in biological material. The method is based on the coloured complex between dithizone and organo-lead compounds. Tetraethyl lead does not react and the complex with triethyl lead may be distinguished from the diethyl lead complex by its absorption spectrum. The method may therefore be made specific for triethyl lead.

The distribution and amount of triethyl lead in certain tissues of rats killed at 4 hr. and 24 hr. after intraperitoneal injections of triethyl lead chloride are given in Table 2. The highest concentrations were found in whole blood. When analyses were made on separated plasma and erythrocytes over 90% of the triethyl lead was found in the erythrocytes. Liver and kidney also contained appreciable quantities of triethyl lead but a lower concentration

was found in the brain. Unlike the results in the other three tissues the amount of triethyl lead found in the brain increased over a 24-hr. period but longer time intervals were not studied. After the administration of tetraethyl lead to rats considerable quantities of triethyl lead were found in the tissues. The pattern of distribution of the triethyl lead was virtually identical to that found after injections of triethyl lead. Again the amount found in brain was less than that found in other tissues.

To determine the stability and persistence of triethyl lead in rat tissues *in vivo* a group of five rats was given triethyl lead chloride, 10 mg./kg. intraperitoneally, and killed at intervals between two hours and four days. The tissues were removed for analysis of triethyl lead. The results in Table 3 show that the level of this compound remained almost unaltered during this time. This persistence may account for the late deaths after single doses.

TABLE 3

PERSISTENCE OF TRIETHYL LEAD IN RATS *IN VIVO*

Time Killed after Injection (hr.)	Brain Cortex Slices (% of controls)			Triethyl Lead (μg./g. wet wt.)		
	QO_2	Lactic Acid	Pyruvic Acid	Blood	Liver	Kidney
2	100	125	95	57	36	17
4	55	330	60	65	39	24
24	53	300	53	35	30	19
48	43	292	51	43	29	26
96	56	270	64	39	22	19

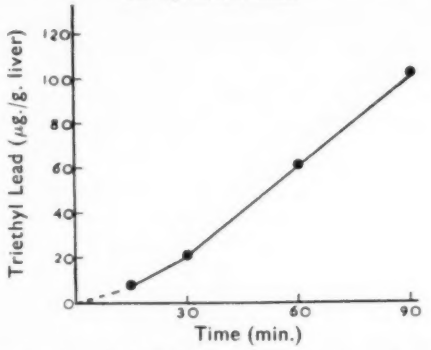
Triethyl lead chloride, 10 mg./kg., was given by intraperitoneal injection.

As stated previously, the recovery of diethyl lead from biological material is low except from blood. Estimations of diethyl lead in blood samples taken from rats which had been given diethyl lead dichloride were made and the results, given in Table 2, indicate that diethyl lead can be found in high con centrations as the intact ion 24 hours after injection.

Conversion of Tetra- to Tri-ethyl Lead.—In previous studies in this laboratory (Cremer, 1958) it was shown that the conversion of tetra- to triethyl tin could be brought about by rat liver *in vitro*.

Therefore several tissues were examined *in vitro* for their ability to convert tetraethyl lead to triethyl lead and the liver was found to be highly active, while negligible activity was found in kidney and brain. When rat liver slices were incubated with tetraethyl lead the amount of triethyl lead produced was proportional to the wet weight of liver used. The rate of production of triethyl lead by liver slices is shown in Fig. 1. This rate of conversion of tetra- to tri-ethyl lead could account for the amount of triethyl lead found in the tissues of rats four hours after an injection of tetraethyl lead (Table 2) asuming that the conversion took place in the liver from

FIG. 1.—The rate of conversion of tetra- to tri-ethyl lead by rat liver slices.



where the triethyl lead formed was distributed throughout the body.

During the past few years several detailed studies have been made on the metabolism of a wide variety of foreign substances by liver preparations (see review by Brodie, 1956). The main factor in common is that the microsomal fraction plus soluble material of the liver cell appears to be the site of activity. The exact location of the active principles concerned is not known, but the major portion of the activity is found in the supernatant remaining after larger particles, which include nuclei and mitochondria, have been removed. The supernatant contains the microsomes and water-soluble cell constituents. Experiments have been carried out on the conversion of tetra- to tri-ethyl lead using fractions of liver homogenates prepared by the usual centrifugation techniques as described in Methods. The distribution of activity is given in Table 4 which shows that the major portion of it was in the microsomes plus soluble material of the cell. When separated fractions of liver cells are used the conversion activity is enhanced by the addition of several fortifying constituents. The maximum activity was obtained with the conditions described in the legend to Table 4. No conversion took place

TABLE 4

DISTRIBUTION IN RAT LIVER CELLS OF SYSTEM CONVERTING TETRAETHYL LEAD TO TRIETHYL LEAD

Liver Fraction	Activity (%)
Whole homogenate	100
Cell debris + nuclei	0
Washed mitochondria	0·4
Microsomes + soluble material	94·5
Unwashed microsomes	3
Soluble material	1·3

Each flask contained a sample (2 ml.) of liver cell fraction in 0·3 M sucrose, tetraethyl lead 0·0007 M, $MgSO_4$ 0·018 M, nicotinamide 0·008 M, triphosphopyridine nucleotide 0·00014 M, and phosphate buffer 0·016 M final concentrations in a total volume of 3·0 ml. with the *p*H adjusted to 6·9. Incubation was at 37°C. in O_2 for 90 min., and determinations of triethyl lead were then made. The activity of the whole homogenate, taken as 100%, was 190 μg. triethyl lead/g. wet wt./hr.

in an atmosphere of 95% N_2 + 5% CO_2 and the reaction was inhibited by the substance SKF525A (diethylamino ethyl diphenyl propylacetate), well known for its ability to inhibit the metabolism of drugs by liver microsomes (Brodie, 1956).

The results from experiments carried out *in vitro* thus confirm that rat liver has the ability to convert tetra- to tri-ethyl lead.

Effect of Lead Compounds on Rat Brain Metabolism *in vitro*.—From the studies of the different lead compounds on rats *in vivo* it was evident that tetra- and tri-ethyl lead produced identical signs of poisoning while diethyl lead and lead acetate were very much less toxic. Biochemical studies on the effect of these lead compounds on the metabolism of brain preparations *in vitro* were performed in an attempt to throw some light on observations made *in vivo*.

Experiments with Rat Brain Brei.—First, experiments were carried out using rat brain brei. This type of preparation consists of a mixture of small clumps of whole, isolated, and disintegrated cells. The preparation actively metabolizes lactic acid, oxidizing it *via* pyruvic acid. An interference in the lactate metabolism is reflected by an alteration in the O_2 consumption and in the level of pyruvate.

The effect of different lead compounds on the utilization of lactate by rat brain brei preparations was examined. Earlier studies by Aldridge and Cremer (1955) showed that by using this technique a difference between the biochemical action of diethyl tin and triethyl tin could be readily detected. They found that concentrations of diethyl tin which lowered O_2 uptake led to an accumulation of pyruvate and in this respect resembled arsenious acid and phenylarsenious acid. Triethyl tin, on the other hand, lowered both O_2 uptake and the pyruvate level. Table 5 shows the results obtained with the lead compounds. Both tetraethyl lead and lead acetate were without effect. Diethyl lead, like diethyl tin, caused an accumulation of pyruvate when O_2 uptake was lowered. The effect of triethyl lead was less clear cut. At high concentrations the O_2 uptake was lowered and there was a small increase in the pyruvate level. At lower concentrations, which still inhibited O_2 uptake, the pyruvate level was decreased. The effects obtained using either di- or tri-ethyl lead at 1×10^{-4} M concentration show that there is a distinct difference between the mode of action of the two compounds.

TABLE 5

EFFECT OF LEAD COMPOUNDS ON RAT BRAIN BREI PREPARATIONS OXIDIZING LACTATE

Lead Compound	Concentration (M)	O_2 Uptake (% of control)	Pyruvate Level (% of control)
Tetraethyl lead	7×10^{-6}	100	86·5
	9×10^{-5}	100	97
Triethyl lead	$4{\cdot}6 \times 10^{-4}$	64	146
	$1{\cdot}5 \times 10^{-4}$	76·5	58
	$5{\cdot}2 \times 10^{-5}$	91	72
Diethyl lead	$3{\cdot}3 \times 10^{-4}$	30	432
	$1{\cdot}1 \times 10^{-4}$	51	298
	$3{\cdot}6 \times 10^{-5}$	79	136
Lead acetate	$1{\cdot}6 \times 10^{-4}$	96	107

Each flask contained lithium lactate 0·015 M, brei equivalent to 17 mg. wet weight of original brain, and inhibitor as indicated. The final volume was made up to 3 ml. with 0·1 M phosphate buffer *p*H 7·4. The centre well contained 0·15 ml. 20% (w/v) KOH for CO_2 absorption. The gas phase was air and the temperature 37°C. After 10 min. equilibration readings were taken every 10 min, up to 50 min. At the end of the experiment 3 ml. 18% (w/v) TCA was added to each flask and 3 ml. samples taken for the estimation of pyruvate.

Diethyl tin has been shown to resemble phenylarsenious acid and lewisite (Stocken and Thompson, 1946) in its avid reaction with B.A.L. but only slight affinity for glutathione (Aldridge and Cremer, 1955). The effect of several SH compounds on the oxidation of lactate by rat brain brei in the presence of di- and tri- ethyl lead has been studied and the results are given in Table 6. The effects of diethyl lead were completely prevented by B.A.L. and almost completely prevented by thioglycollic acid whereas glutathione had only a slight effect. On the other hand these thiol compounds had no effect upon the action of triethyl lead.

TABLE 6

EFFECT OF SH COMPOUNDS ON OXIDATION OF LACTATE BY RAT BRAIN BREI IN PRESENCE OF DI- AND TRI- ETHYL LEAD

Concentration of Organo-lead Compound (M)	Concentration of SH Compound (M)	R	O_2 Uptake (% of control)		Pyruvate (% of control)	
			Inhibitor	Inhibitor + SH Compound	Inhibitor	Inhibitor + SH Compound
Diethyl lead $1{\cdot}1 \times 10^{-4}$	B.A.L. $2{\cdot}8 \times 10^{-4}$	2·5	49	100	298	100
$1{\cdot}1 \times 10^{-4}$	Thioglycollic acid $3{\cdot}7 \times 10^{-4}$	3·4	52	81·5	278	117
$1{\cdot}1 \times 10^{-4}$	Glutathione 6×10^{-4}	5·5	43	56	408	246
Triethyl lead $2{\cdot}5 \times 10^{-4}$	B.A.L. 3×10^{-4}	1·2	76	77	69	80
$2{\cdot}5 \times 10^{-4}$	Thioglycollic acid $3{\cdot}0 \times 10^{-4}$	1·2	76	68	67	61
$2{\cdot}5 \times 10^{-4}$	Glutathione $3{\cdot}8 \times 10^{-4}$	1·5	72	72	58	50

The procedure was the same as described for Table 1. SH compounds and the organo-lead compounds were added as indicated and left 10 min. at room temp. before 1 ml. of brain brei was added. R is the quotient of the molar concentration of SH compound/molar concentration of organo-lead compound.

Experiments with Slices of Rat Brain Cortex.—Preparations of rat-brain cortex slices have also been used. The slices were incubated in Krebs-Ringer phosphate medium with glucose as substrate. As with the rat brain brei experiments, any alteration in the O_2 consumption or levels of intermediate compounds normally present during the oxidation of glucose is indicative of a biochemical lesion.

The effects of the four lead compounds on this system were studied (Table 7). The most active was

TABLE 7

EFFECT OF LEAD COMPOUNDS ADDED *IN VITRO* ON METABOLISM OF SLICES OF RAT BRAIN CORTEX

Lead Compound	Concentration (M)	% of Control		
		QO_2	Lactic Acid	Pyruvic Acid
Tetraethyl lead	2×10^{-4}	90	163	88
	7×10^{-5}	100	100	100
Triethyl lead	2×10^{-6}	45·5	355	38
	7×10^{-7}	86	285	66
+ E.D.T.A. 8×10^{-5} M	7×10^{-7}	86	315	51
Diethyl lead	1×10^{-5}	42	153	48
	3×10^{-6}	100	110	82
Lead acetate	2×10^{-4}	100	110	100

The control values for lactic acid and pyruvic acid were 193 μg. and 11 μg. respectively, estimated as the amount present in the medium after 75 min. incubation, and E.D.T.A. was added as ethylenediamine-tetra-acetic acid disodium salt.

triethyl lead, which caused a lowering of the O_2 consumption and the pyruvate level with an increase in the lactate level. This effect was identical with that previously shown for triethyl tin (Cremer, 1957). The altered metabolic pattern suggested that the oxidation of pyruvate to CO_2 and water was impaired and that the system had become partially anaerobic causing pyruvic acid to be reduced to lactic acid which accumulated. During the complete oxidation of glucose the major part of the synthesis of energy-yielding substances, in particular phosphocreatine and adenosine triphosphate, occurs during the oxidation of pyruvate *via* the tricarboxylic acid cycle.

There was an interesting difference between the sensitivity of brain brei preparations and brain slices to triethyl lead. Brain slices were over a hundred times more sensitive. Although the reason for this difference is not understood it is an important factor to be borne in mind when testing the action of toxic substances *in vitro*. Unpublished observations by W. N. Aldridge in these laboratories indicate that oxidation coupled to phosphorylative processes of isolated rat liver mitochondrial preparations is sensitive to triethyl lead at a concentration of 5×10^{-7}M.

Tetraethyl lead was without effect except at concentrations over a hundred times greater than those of triethyl lead. The small activity at these higher concentrations might have been due to traces of triethyl lead as a contaminant.

Diethyl lead was less active than triethyl lead. A distinguishing feature between the two compounds was that when the O_2 uptake was inhibited and the pyruvate lowered by either compound the concomitant increase in lactic acid was always far greater in the presence of triethyl lead. Lead acetate was without effect.

Activity of Brain Slices Prepared from Rats Given Lead Compounds.—Slices were prepared from the brains of rats given lead compounds and their metabolic activities are recorded in Table 2. There was a marked alteration in the metabolism of brain slices taken from rats which had been given tetraethyl lead and triethyl lead. The inhibition of the O_2 uptake, increase in lactate, and decrease in pyruvate was identical with that of brain slices to which triethyl lead was added *in vitro* (Table 7). Estimations were also made of the amount of organo-lead compounds in some of the tissues of these animals. There was quite a close correlation between the amount of triethyl lead in the tissues and the extent of alteration in the metabolism of brain slices after administering either tetra- or tri-ethyl lead. An important difference between the two is that nearly double the dose of tetraethyl lead was required to produce effects equivalent to those of triethyl lead. In an attempt to confirm whether, in each case, the altered metabolism of the brain slices was due to the presence of triethyl lead, separate groups of rats were injected with either tetra- or tri-ethyl lead and brains removed for triethyl lead analysis. Although the amount found in the brain is low compared with other tissues, since brain slices are very sensitive to triethyl lead, the amount of this substance in the brain *in vivo* is sufficient to account for the altered metabolic activity seen *in vitro*. This is shown more clearly in Table 8 where the concentrations have been expressed as molarity. The assumption has

TABLE 8

COMPARISON OF ACTIVITY OF BRAIN SLICES WITH TRIETHYL LEAD ADDED *IN VITRO* AND SLICES FROM RATS GIVEN EITHER TETRA- OR TRI-ETHYL LEAD *IN VIVO*

Route of Administration of Organo-lead Compound	Concentration of Triethyl Lead in Brain Tissue Fluid (M)	Brain Cortex Slices (% of control)		
		QO_2	Lactic Acid	Pyruvic Acid
Triethyl lead *in vitro*	$1·6 \times 10^{-6}$	86	285	66
	$4·6 \times 10^{-6}$	45·5	355	38
Triethyl lead *in vivo*	$1·8 \times 10^{-6}$	54·5	330	58·5
	$3·4 \times 10^{-6}$	53	300	52
Tetraethyl lead *in vivo*	$1·02 \times 10^{-6}$	50	295	46
	$8·15 \times 10^{-6}$	33	280	36

been made that all triethyl lead found is in the tissue fluid of the brain, taking this value as 80% of the wet weight. Unpublished observations have shown that when brain slices are incubated with triethyl lead *in vitro* the concentration found within the

slice is 23 times greater than that originally added in the medium. This factor has been used to calculate the amount of triethyl lead in the tissue fluid of brain slices when added *in vitro*. The metabolic activities are taken from Tables 2 and 7. Although the results show a good correlation, the values for the data *in vivo* are necessarily only approximate because of the assumptions which have been made in the calculation and the use of different groups of rats.

There was some alteration in the metabolism of brain slices taken from rats given diethyl lead dichloride, 40 mg./kg., when killed after 24 hours. The effect was less marked than those of triethyl lead. After a dose of 20 mg./kg. the values were no different from the controls (Table 2).

The metabolic pattern of brain slices prepared from rats given lead acetate, 100 mg./kg., was different inasmuch as there was a small but consistent increase in both the lactate and pyruvate levels without any alteration in the O_2 consumption.

Since rats injected with lead acetate lost weight, which might have been due to a reduction in food intake or poor utilization of ingested food, the activity of brain slices prepared from rats which had been starved for 48 hours was examined. Their metabolic activity was identical with that of slices prepared from fed animals.

Tissue Water Content of Brain and Spinal Cord in Rats Given Triethyl Lead.—A striking feature of rats given tetra- or tri-ethyl tin either in single doses or by addition to the diet is the development of an oedematous lesion in the white matter of the brain and spinal cord. The experimental production of this lesion has been fully described by Magee, Stoner, and Barnes (1957) and a relationship was inferred between the presence of oedema and the alteration of brain metabolism (Cremer, 1957). Owing to the similarity between triethyl tin and triethyl lead in their action on rat brain metabolism it was of interest to know whether triethyl lead caused a similar type of lesion.

A group of eight rats was given 2 mg./kg. triethyl lead chloride intraperitoneally every four days for 36 days. Rats were killed in pairs between one and five weeks and the time was selected so that three days had elapsed since the last injection for each group. Brain slices were prepared from one half for the determination of metabolic activity and the water content determined on the other half. The amount of triethyl lead in the tissues was also measured (Table 9). There was no change in the water content of either the brain or spinal cord of rats given chronic injections of triethyl lead but there was a marked effect on the metabolism of brain slices.

Histological examination of the spinal cords of these animals did not reveal any pathological changes.

Discussion

Throughout reports in the literature on tetraethyl lead poisoning there are conflicting views on whether tetraethyl lead has an action peculiar to its organic nature or whether it acts solely by virtue of its lead content, the only difference from inorganic lead being the ease by which lead in an organic form is absorbed.

The reports by Cassells and Dodds (1946) of 25 cases of tetraethyl lead poisoning showed that the predominant symptoms were disturbances in the central nervous system, low blood pressure, and lowered body temperature. Abdominal colic, stippling of the red cells, and punctate basophilia, well known symptoms of inorganic lead poisoning, were seldom seen. Symptoms developed within a few days after exposure and unless death occurred during this acute period recovery was fairly rapid and complete.

These authors state that "the toxicity of tetraethyl lead is a function of the lead content and not of any peculiar qualities characteristic of the compound, but its fat-soluble character allows selective localization in the nervous tissue of the body and for this reason poisoning is essentially a central nervous system intoxication." The results reported in the present work are in conflict with both of these concepts.

Although the rat is the only species of animal which has been used, and it was shown by Calvery, Laug, and Morris (1938) that the rat is relatively insensitive to experimental inorganic lead poisoning, tetraethyl lead poisoning in the rat closely resembles that described for humans.

The symptoms observed in rats injected with the

TABLE 9

WATER CONTENT OF BRAIN AND SPINAL CORD OF RATS GIVEN CHRONIC INJECTIONS OF TRIETHYL LEAD

Duration of Injections (weeks)	Water Content		Brain Slices (% of control)			Triethyl Lead (μg./g.)		
	Brain	Spinal Cord	QO_2	Lactic Acid	Pyruvic Acid	Blood	Liver	Kidney
Control	77·2	69						
1	—	—	60	211	48	17	23	14
2	78	71·7	51	201	41	24	27	19
3	77·4	69·8	47	208	48	26	30	18
5	77·4	69·8	46	254	46	32	37	23

different lead compounds confirmed the findings of Buck and Kumro (1930) that those which develop after tetraethyl lead and triethyl lead are identical and differ from those of diethyl lead and lead acetate.

The concept that the predominance of nervous symptoms is due to the fat-soluble nature of tetraethyl lead causing it to be selectively localized in nervous tissue has not been supported by analytical data. Kehoe and Thamann (1931) found that in rabbits, after the application of tetraethyl lead to the skin, although there was complete absorption, no volatile lead (tetraethyl lead) was found in the central nervous system, but after three hours non-volatile lead began to accumulate. Mortensen (1942) found that the small amount of volatile lead originally present in the brains of rats after inhalation of tetraethyl lead vapour completely disappeared within a few hours.

Several workers have suggested that tetraethyl lead is rapidly broken down in the tissues to water-soluble, non-volatile products (Kehoe and Thamann, 1931; Machle, 1935; Mortensen, 1942). The development of a method using dithizone, described in this paper, which measures triethyl lead as the complete mono-valent organo-lead ion has made it possible to demonstrate directly that tetraethyl lead is broken down to triethyl lead in rats *in vivo*. Triethyl lead appears to be stable in the body for at least four days (Table 3) so that any subsequent degradation to diethyl lead or inorganic lead takes place more slowly than the initial conversion of tetra- to tri-ethyl lead.

Although it was necessary to inject more tetraethyl lead than triethyl lead in order to kill rats, the amount of triethyl lead found in the brain was the same. This suggests that the toxicity of tetraethyl lead is due to its conversion to triethyl lead and only the latter is active.

Although tetraethyl lead is fat-soluble, triethyl lead is strongly water-soluble, as shown in Table 10, and yet it can be found in rat brain tissue *in vivo* and has a strong effect on brain slice metabolism *in vitro*.

It is possible that tetraethyl lead reached the brain in sufficient quantity to enable it to be converted to active concentrations of triethyl lead.

TABLE 10

DISTRIBUTION OF TRIETHYL LEAD CHLORIDE BETWEEN WATER AND VARIOUS SOLVENTS

Solvent	R = Water/Solvent
Chloroform	38·4
Benzene	> 100
Ether	8·0
Olive oil	20·8

R is the quotient of the amount of triethyl lead in the water layer/the amount in the solvent layer. Each R value is the mean obtained when 10 ml. portions of water containing a range of 35 to 150 μg. triethyl lead chloride were mixed with 10 ml. portions of a solvent.

However, this seems unlikely, not only from the analytical data for volatile lead mentioned above but also because when several rat tissues were tested *in vitro* for their ability to convert tetra- to triethyl lead no activity was found in brain whereas a very active system was present in liver. It may be concluded that tetraethyl lead is not concentrated in the brain but rather is converted by the liver to triethyl lead which is transported to the brain.

Experimental findings on the conversion of tetraethyl lead by liver preparations showed that the system has many features in common with the enzymic system(s) responsible for the metabolism of barbiturates, organophosphorus compounds, tetraethyl tin, and several other substances foreign to the body. The conditions which most closely simulate those present *in vivo* for the conversion activity of the liver are not known. The rate found with liver slices of 60 μg. triethyl lead/g. wet weight/hr. would be sufficient to account for the triethyl lead present *in vivo* four hours after injections of tetraethyl lead but the conversion activity was very much higher in fortified liver homogenate preparations where a rate of 190 μg. triethyl lead/g. wet weight/hr. was found.

The biochemical results obtained from studies *in vitro* on the action of tetra-, tri-, and di-ethyl lead and lead acetate on the metabolism of rat brain preparations show that there is a definite difference between the action of these four lead compounds. Tetraethyl lead and lead acetate are without effect when added to brain tissue *in vitro*. The negative results with lead acetate were in contrast to those of Dolowitz, Fazekas, and Himwich (1937) who found that the O_2 consumption and glycolysis of brain tissue was inhibited 50% by lead acetate. The species used by them is not stated and the concentration of lead acetate added to the tissues was high, although, as the authors stated, most of the lead was precipitated by the chloride and phosphates of the suspending fluids. They suggested that the infinitesimal amount of lead that remained free was sufficient to produce effects on tissue metabolism. Since inorganic lead is known to be among the heavy metals which denature proteins, caution must be used when interpreting results where enzyme systems are exposed to high concentrations of such metals. In an experiment carried out in this laboratory using a rat brain homogenate preparation with glucose as substrate, the O_2 consumption was found to be 20% inhibited by lead acetate at a concentration of 9×10^{-4} M but there was no inhibition at 4×10^{-4} M.

The biochemical actions of diethyl lead dichloride and triethyl lead chloride are also different. The action of diethyl lead on brain brei preparations can

be prevented by the addition of B.A.L. or thioglycollic acid showing that this compound has an affinity for SH compounds. Its biochemical behaviour resembles that of phenylarsenious acid, arsenite, and diethyl tin dichloride (Aldridge and Cremer, 1955). Triethyl lead has no affinity for thiol compounds. It is the most active of the four lead compounds against the metabolism of brain slices. Unpublished observations showed that slices of liver and kidney tissue were less sensitive to triethyl lead than brain. Although the action of triethyl lead on the metabolism of rat brain cortex slices is indicative of an impairment of glucose oxidation and consequently a reduction in the synthesis of high-energy phosphates, no experimental studies have as yet been made to confirm whether it has a similar action *in vivo*. The biochemical effects of di- and triethyl lead appear to be very similar to those of di- and tri-ethyl tin respectively, and considerable detailed studies on the toxicity of di-and tri-alkyl tin compounds have been made in these laboratories as was recently reported by Barnes and Stoner (1958). The exact mode of action of triethyl tin is not yet known, but from the study on the metabolism of phosphate compounds in brain *in vivo* (Stoner and Threlfall, 1958) of rats injected with triethyl tin it seems that there is a failure in the utilization of chemical energy rather than in its production. A similar finding might be true for triethyl lead, but not necessarily because the signs of poisoning by the two compounds are not identical in rats *in vivo*.

It is important to note that tetraethyl lead is without effect on the metabolism of brain cortex slices when added *in vitro*, except at high concentrations. This negative effect provides almost conclusive evidence that the deranged metabolism of brain slices prepared from rats which have been given tetraethyl lead is due entirely to the triethyl lead shown to be present in the brains of these animals. Calculations made from Table 8 show the possibility of a correlation between the amount of triethyl lead found in the brains of animals injected with either tetra- or triethyl lead and the degree of alteration to the metabolism of brain slices.

From the chemical nature of tetraethyl lead it would not be expected to be a reactive compound in the body. However, its conversion to triethyl lead appears to be readily brought about by an enzyme system(s) in liver although the mechanism of the reaction is not known. The product, the monovalent triethyl lead ion, is biochemically active, particularly against brain tissue, and does not undergo rapid decomposition by the liver.

The effect of triethyl lead on brain metabolism appears to be due to its organic lead composition and not primarily to its lead content.

Studies on the metabolism of substances foreign to the body have shown that in many instances the product is more toxic than the original compound so that the term "detoxication mechanism" is not applicable. This seems to be the case for tetraethyl lead.

No effective treatment can be suggested for tetraethyl lead poisoning. Although SKF 525-A prevented the conversion *in vitro* of tetra- to tri-ethyl lead it has not been tested *in vivo* for possible therapeutic value. However, it did not prevent the conversion of tetra- to tri-ethyl tin in rats *in vivo* (Cremer, 1958).

Kitzmiller, Cholak, and Kehoe (1954) treated men suffering from tetraethyl lead exposure with ethadamil-calcium-disodium (the calcium salt of E.D.T.A.) and compared its effectiveness with B.A.L. They found that no valid conclusions could be drawn as to the useful therapeutic effects, but both substances increased the output of inorganic lead in the urine. Since it has been shown in this paper that triethyl lead does not combine with either E.D.T.A. or B.A.L. it is unlikely that they would be effective in preventing its action. A substance which did combine avidly with triethyl lead might prove to have more therapeutic value in tetraethyl lead poisoning.

I wish to thank Dr. P. R. Boyd of the Associated Ethyl Company Ltd. for his kind cooperation and for supplying tetra-, tri-, and di- ethyl lead, Mr. D. Potter for invaluable technical assistance, and Dr. P. N. Magee for examining the histological preparations.

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DERMATITIS IN THE SOUTH WALES MINING INDUSTRY: A REPORT OF A SURVEY OF TWO COLLIERIES

BY

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From the Welsh National School of Medicine, Cardiff

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A survey to determine the prevalence of dermatitis in collieries and to investigate the aetiology of the condition has been carried out in South Wales.

Two collieries were chosen because of a marked variation between them in the incidence of claims for dermatitis compensation. The method was to examine the entire colliery populations and to submit the cases found to detailed study.

The populations consisted of all miners on the colliery pay-rolls on the day the survey began. Of both populations practically 100% were examined.

The cases were classified as occupational and non-occupational, and a third group was reserved for doubtful cases possibly related to occupation. The prevalence of occupational dermatitis was almost the same in the two collieries. The prevalence of non-occupational dermatitis was also similar in the two collieries. The incidence of claims for benefit does not therefore appear to reflect the true prevalence of the disease. A correlation between the contrasting claims rates and variation in the severity of occupational dermatitis in the two collieries was established.

Occupational dermatitis most commonly developed on the lower limbs; this tendency was greatest in coal-face workers. The special distribution of the rash corresponded to the areas most exposed to frictional damage at work.

This report presents the results of a survey of two collieries in which the main objectives were to measure the prevalence of dermatitis, and to investigate the aetiology of the disease.

The reason for investigating two collieries must be given. The measurement of prevalence in one colliery is to some extent an end in itself, but by establishing differences in prevalence in two, clues about the aetiology of dermatitis might be furnished with greater readiness.

Choice of Collieries

In planning an investigation into a disease with a relatively low prevalence the collieries selected must provide a reasonable hope of obtaining differences which are significant. Therefore a search was made for two collieries in which there was evidence that the prevalence of dermatitis could be expected to be high in one and low in the other.

A miner who contracts dermatitis which he contends is due to his employment may under the National Insurance (Industrial Injuries) Acts claim benefit. The claim that his incapacity is due to a prescribed industrial disease is made at the time a first medical certificate is received. This form is sent to the local insurance officer, who notifies the colliery at which the claimant is employed. The total of claims recorded at the colliery is published monthly and includes claims lodged by men with first attacks as well as by those with recurrences of dermatitis.

Since the number of claims in individual collieries offered a guide to the prevalence in them of dermatitis, the selection of suitable collieries was primarily based on an examination of these records.

A short list of eight neighbouring collieries was first made. These collieries were chosen because they had in common two features which, it was realized, would render the actual surveys more easily possible. First, each contained a stable labour force of approximately 1,000, and secondly, they all had pit-head baths and medical centres.

The average number of claims in the eight

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collieries on the short list for the 18-month period preceding the surveys was 24·0 per thousand employed. Since the highest value was 39·0 in one colliery and the lowest 15·8 in another, these collieries, hereafter referred to as " high claim " colliery and " low claim " colliery respectively, were therefore the two selected for the present investigation.

It must be stressed that while it was appreciated that the number of claims for dermatitis compensation in the eight short-listed collieries might be considerably influenced by differing diagnostic standards among the medical practitioners responsible, there was no evidence of serious variation among the practitioners concerned with the claims arising in the two collieries finally selected.

Detailed Objectives

The detailed objectives were (1) to examine for evidence of dermatitis as large a percentage of the two colliery populations as possible. In dealing with a disease of relatively low prevalence it was important in surveying two populations each of the order of 1,000 workmen to examine them all. (2) To measure the real prevalence of dermatitis in the two collieries. Though emphasis was placed on the measurement of the prevalence of occupational (miner's) dermatitis, other forms of dermatitis unrelated to occupation were to be expected and their prevalence was measured. (3) To investigate the aetiology of occupational dermatitis in miners. In non-mining industries occupational dermatitis is primarily an exogenically determined condition. In miners the skin is constantly exposed to a variety of external physical hazards. Chief among these are frictional damage from dust and maceration by water and sweat. The third objective, therefore, was to investigate in miners the role of these factors in the aetiology of occupational dermatitis, and the problem was faced in two ways.

(*a*) Should the prevalence of occupational dermatitis as measured in the two surveys vary significantly and confirm the contrasting incidence of the claims for dermatitis compensation, then a careful comparison of environmental conditions below ground in both collieries might identify those factors primarily responsible for the condition. As the surveys showed a closely similar prevalence of occupational dermatitis in the two collieries (see Results), the aetiology was not investigated in this way.

(*b*) If external physical factors are the main cause of miner's dermatitis, then it follows that the highest prevalence would be expected in workmen most exposed to these hazards. This theory could be tested in the populations surveyed by contrasting the prevalence in workmen below ground with that measured in surface workers.

Among manual workers in an engineering factory, Squire, Cruickshank, and Topley (1950) found that hands and forearms, the sites most exposed to injury, were most commonly affected by skin disease. If it were found that in mineworkers also dermatitis developed most frequently in those anatomical areas most exposed to the action of external physical agents, the aetiological significance of these factors would be strengthened.

Descriptive Background

The two collieries chosen for the investigation are situated in the county of Glamorgan. Both stand in small, secluded, rural valleys about 10 miles apart. " High claim " colliery workmen come mainly from a moderately large mining town one mile away, while those employed at " low claim " colliery live in neighbouring villages.

The main " coaling " or " day " shift provides work for two-thirds of the total personnel in both collieries, the " afternoon " and " night " shifts employing the remainder in approximately equal numbers. Using similar methods and at equal depths of 1,800 feet, machine-cut and hand-loaded steam coal (volatile matter, 13-16%) and bituminous coal (volatile matter, 23-26%) are extracted at " high claim " and " low claim " collieries respectively. The average height of the seams worked in " high claim " colliery is 4 ft., in " low claim " colliery 5 ft., and the suppression of dust at source in all working faces is efficient.

The gradients of temperature to which miners are exposed while travelling to and from their various places of work underground were measured in the two collieries. In the September that the underground atmospheric environment was studied, " high claim " colliery pit bottom (" downcast ") dry-bulb temperature was 60° F. and " low claim " colliery 57° F. In the first colliery the temperatures at the coalfaces varied between 70° F. and 74° F., while in the second they ranged from 67° F. to 74° F.

The effective temperature index which combines the three characteristics of an environment, namely, dry-bulb and wet-bulb temperatures, and the rate of air movement, was also measured in the two collieries. In travelling from " high claim " colliery pit-bottom to the various coalfaces, increases of from 14° F. to 20° F. in effective temperature were experienced, while in " low claim " colliery the corresponding increases were from 12° F. to 22° F.

Both collieries have pit-head baths and under the same roof a medical centre in the charge of a state registered nurse.

The Defined Colliery Populations

The two populations consisted of all miners on the colliery pay-rolls except those absent from work for more than 12 months. An index giving the name, colliery registration number, age, and occupation of each workman was prepared from this source at both collieries, the final defined population being the one that existed on the day the survey began.

The two populations are compared in Fig. 1, and their composition in terms of broad work categories is shown in Table 1.

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DEFINED COLLIERY POPULATIONS ANALYSED BY OCCUPATION

Colliery	Total Population	Underground Workmen				Surface Workmen
		Colliers	Other Face-workers	Elsewhere	Total	
"High claim"	1,017	190	295	325	810	207
"Low claim"	1,074	208	288	406	902	172

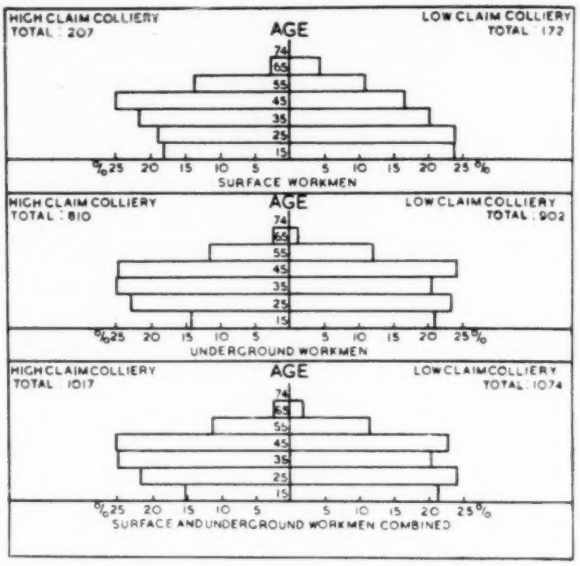

FIG. 1.—Defined colliery population analysed by age.

General Methods of Work

"High claim" colliery was surveyed between August and December, 1954, and "low claim" colliery between February and June, 1955.

Lectures and informal talks with the Colliery Consultative Committee members explaining the scheme were started about a fortnight before the actual surveys. In addition, verbal and written propaganda was widely distributed throughout the collieries.

The actual surveying was done in two stages.

Screening for Dermatitis.—The object of this stage was to identify miners affected with dermatitis. To do this it was necessary to examine stripped and clean all members of the defined populations. This stage, therefore, was mainly carried out in the pit-head baths which at both collieries were used by more than 80% of miners.

In the baths each workman has two lockers, one for street clothes, the other for work clothes. Both "clean" and "dirty" lockers are arranged in 14 bays each containing 72 lockers. Every miner was examined for evidence of dermatitis beside his "clean" locker, generally after he had completed his shift and was about to dress for home after bathing. The name and colliery registration number of each man was recorded on a cyclostyled form, together with the results of the cutaneous inspection. The whole procedure occupied about three minutes. The names of those examined were then removed from the population index. A fresh bay was examined daily, and when the last was completed, approximately 75% of the defined populations had been screened for the presence of dermatitis.

To facilitate this stage, the busiest of the surveys, it was necessary to adopt a daily programme to account for the three workshifts. Miners completing the day shift were mainly examined between 2 and 3.30 p.m., those completing the afternoon shift betwen 10 and 11 p.m., and night shift workers between 6 and 7 a.m. As the largest volume of work coincided with the conclusion of the day shift, the burden was eased by screening a proportion in the mornings before the start of the shift.

Approximately 20% of miners in both collieries bathed at home. These men, together with a few who were overlooked in the pit-head baths, were examined, before they started work, in the doctor's room at the colliery medical centre. By arrangement with the management, surface men engaged in clean work were often examined during the course of their shifts. Finally, a small minority were visited at their homes or in hospital.

Special arrangements were made to examine members of the populations terminating employment during the surveys. Through the cooperation of the management these workmen attended the medical centre for interview before their discharge from the colliery.

Irrespective of duration or morphology, the presence of dermatitis admitted a miner to the second stage of the survey.

Special Interview and Evaluation.—Miners with any skin disease detected at the preliminary screening were asked to attend the colliery medical centre. At this second interview of between 15 and 30 minutes it was first necessary to decide whether the rash each miner presented was significant for the purpose of measuring prevalence. Except where there was a history of past dermatitis, the existing rash was considered significant only when it had run a course of not less than seven days. In practice few cases—three in "high claim" colliery, five in "low claim" colliery—were inadmissible for this reason.

Diagnostic Criteria.—It is customary to classify dermatitis according to aetiology. In this survey of

working miners, the cases of dermatitis found by the preliminary screening were divided in the first instance into two broad groups: occupational dermatitis, in which the physical environment in mining was considered to be the chief aetiological factor, and non-occupational dermatitis, in which factors independent of mining were of greater importance.

(1) *Occupational Dermatitis.*—It must be stressed that while it was realized that in epidemiological surveys it is essential that the findings of different observers should be comparable, it was nevertheless difficult in the present investigation to arrive at satisfactory criteria on which to base the diagnosis of occupational dermatitis. Specific risks to the skin in non-mining industries are well known, and accurate diagnostic standards incorporating the added objective evidence of patch-testing are readily furnished. In miners, on the other hand, the natural history of occupational dermatitis is not yet clear, and therefore in the present investigation the diagnosis was assessed on subjective evidence alone.

The diagnosis was based upon a characteristic history of a rash, generally pruritic, first developing during employment as a miner, with evidence of recovery or improvement after withdrawal from the causative environment, with or without relapse or recurrence on returning to it. The cases which satisfied these criteria were then divided into the following three groups:

(*a*) Traumatic (non-specific) eczematous dermatitis; (*b*) contact sensitization dermatitis resulting from personal allergy to some external contact at work; (*c*) eczematous dermatitis, arising from aggravation by occupation of a predisposing constitutional eczema.

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In miners it was to be expected that difficulty in excluding an occupational factor would arise. A third group was therefore reserved for cases of dermatitis of doubtful aetiology but in which it was possible that occupational factors played a contributory part in causation.

Groups Studied.—Seventy-one miners in " high claim " colliery and 73 in " low claim " colliery were interviewed and examined at this stage of the survey. Of these, 29 at each colliery were considered to be cases of occupational dermatitis and they form the principal groups studied in this report.

The cause was in doubt in 22 cases of dermatitis in " high claim " colliery and in 23 cases in " low claim " colliery. Because of this uncertainty it was considered unwise to draw detailed conclusions from a study of these groups, and the results presented for them are correspondingly less important.

Dermatitis assigned to the non-occupational group was represented by 20 cases in " high claim " colliery and 21 in " low claim " colliery. The cases in these groups were classified according to the specific diagnosis, but in both collieries the final numbers in each class were too small to permit detailed analysis.

Results

The Populations Examined.—Practically 100% of both populations were examined (99·8% " high claim " colliery; 99·9% " low claim " colliery). Of those miners not examined, one in each colliery died before an interview was arranged, and during the " high claim " colliery survey two men, one with a hemiparesis and the other with abdominal carcinomatosis, were not examined.

Most of the examinations were made on the colliery premises (96·3%, " high claim " colliery; 97·3%, " low claim " colliery). The rest were conducted either in the home or hospital, and it was found that fewer home visits to absentees were necessary in surveying " low claim " colliery. It was easier for the ambulant sick in this colliery to attend the medical centre for examination since their homes were generally nearby. Most " high claim " colliery workmen, on the other hand, lived at a greater distance from their work, and therefore it was usually more convenient to visit an absentee at his home. Six mineworkers were examined in hospital during the two surveys.

Prevalence of Occupational Dermatitis.—Table 2 shows the prevalence of occupational dermatitis in the populations surveyed, and also compares the prevalence of the three principal types of the condition. The most striking feature is the close similarity of the prevalence in the two colliery populations. Traumatic eczematous dermatitis, quantitatively similar in the two collieries, predominates over contact sensitization dermatitis and constitutional eczema materially aggravated by occupation, which together form a very small part of the total prevalence. Hodgson (1955) pointed out that specific hazards to the skin in the mining industry are few, and in a series of 404 Welsh miners found a corresponding paucity of cases of occupational dermatitis resulting from sensitivity to rubber and other chemicals, or to oil, greases, and alkali. Similarly, among the miners with occupational dermatitis in the two populations now surveyed, only one was considered to be a case of specific sensitization

TABLE 2

PREVALENCE OF OCCUPATIONAL DERMATITIS IN POPULATIONS SURVEYED, ACCORDING TO THREE PRINCIPAL CLINICAL TYPES

Colliery	High Claim (Pop. surveyed, 1,014)		Low Claim (Pop. surveyed, 1,073)	
Clinical type	No.		No.	
Traumatic eczematous dermatitis	27	(2·7%)	27	(2·5%)
Contact sensitization dermatitis	—		1	
Aggravation of constitutional eczema	2		1	

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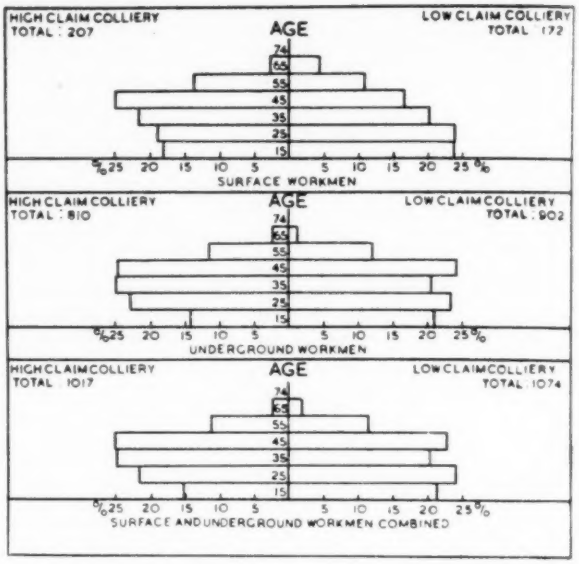

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TABLE 3

PREVALENCE OF OCCUPATIONAL DERMATITIS AMONG THE SURFACE AND UNDERGROUND WORKERS EXAMINED

Colliery	Coalface Workers		Men Employed Elsewhere below Ground		Surface Workers		Total	
	No. Examined	No. of Cases	No. Examined	No. of Cases	No. Examined	No. of Cases	No. Examined	No. of Cases
"High claim"	485	13 (2·7%)	322	14 (4·4%)	207	2 (1%)	1,014	29 (2·9%)
"Low claim"	496	14 (2·8%)	405	13 (3·2%)	172	2 (1·2%)	1,073	29 (2·7%)

(patch test positive) dermatitis, the result of contact with rubber at work.

Occupational dermatitis of the type resulting from aggravation of a constitutional eczema was found in three miners among the populations examined; moderately severe seborrhoeic dermatitis was the underlying predisposing disorder common to all three.

Relationship with Occupation.—The colliery populations examined were divided into three broad occupational groups: coalface workers, miners employed elsewhere below ground, and surface workers. The prevalence of occupational dermatitis among these three groups is shown in Table 3. The prevalence in the miners employed below ground and away from the coalface appears slightly higher than that in the faceworkers. Unfortunately the number of cases in the two groups is small, and the observed difference is not significant. The surface workers were less commonly affected by occupational dermatitis. In each colliery, the difference between the prevalence in surface workers and that in workers below ground is barely statistically significant, but when the figures in the two collieries are combined the results, while not conclusive, are at least suggestive. It is probable that the risk of occupational dermatitis is greatest below ground, where physical hazards to the skin are more frequent.

Age at Onset of First Attack.—An analysis in terms of age at the time of the first attack is shown in Table 4 for the workmen below ground with occupational dermatitis. As there was no significant variation in prevalence between coalface workers and men employed below ground away from the face, the cases of occupational dermatitis in the two groups are treated together. Moreover, as the actual age at the time of onset of the first attack was often in doubt, and also because of the small numbers involved, the cases are grouped in 10-year age groups. It will be seen that most cases of occupational dermatitis first developed in the age groups 35-44 and 45-54, these groups together accounting for 74% and 63% of the total cases in the two collieries. This confirms the observation of Rook and Hodgson (1954) that dermatitis in coal-miners principally develops in the two decades between 40 and 60.

TABLE 4

PERCENTAGE DISTRIBUTION OF CASES ACCORDING TO AGE AT TIME OF ONSET OF FIRST ATTACK IN UNDERGROUND WORKERS WITH OCCUPATIONAL DERMATITIS

Age (years)	"High Claim" Colliery	"Low Claim" Colliery
	No. of Cases	No. of Cases
15	1 (4%)	3 (11%)
25	2 (7%)	4 (15%)
35	14 (52%)	7 (26%)
45	6 (22%)	10 (37%)
55–64	4 (15%)	3 (11%)

Chief Sites of Onset in First Attack.—The relative frequency with which lesions first appeared on different parts of the body in the underground workers with occupational dermatitis is shown in Table 5. Because of the small numbers the cases at both collieries have been combined. When lesions appeared in the first attack simultaneously at more than one site, the part most affected was recorded as the chief site of onset. The following tentative suggestions are made: (1) Occupational dermatitis in the first attack most commonly develops on the lower limbs, particularly in the region of the feet and ankles. (2) Among coalface workers these sites are more frequently affected than in men employed away from the face. (3) The reverse relationship holds for the frequency with which dermatitis develops on the hands and forearms in the two occupational groups. Hodgson (1955) reported a similar preponderance of origin on the lower limbs in a series of miners. The external physical factors

TABLE 5

CHIEF SITES OF ONSET OF FIRST ATTACK OF DERMATITIS IN COALFACE WORKERS AND MEN EMPLOYED ELSEWHERE BELOW GROUND

Chief Site of Onset	Coalface Workers	Men Employed Elsewhere below Ground
	No.	No.
Dorsa feet and ankles	11 (41%)	7 (26%)
Lower legs	6 (22%)	6 (22%)
Thighs	5 (18%)	0
Hands and forearms	4 (15%)	10 (37%)
Neck and shoulders	1 (4%)	4 (15%)

responsible for the precipitation of dermatitis may exert their main influence on these areas. The place and nature of employment below ground also appear to influence the part of the body initially affected.

Duration of Exposure.—Table 6 compares the approximate duration of underground employment up to the time of onset of the first attack in workers below ground in the two collieries. Again because

TABLE 6

DURATION OF EXPERIENCE BELOW GROUND AT ONSET OF FIRST ATTACK IN UNDERGROUND WORKERS WITH OCCUPATIONAL DERMATITIS

Total Experience below Ground (years)	" High Claim " Colliery	" Low Claim " Colliery
0–	1 (4%)	4 (15%)
10–	4 (15%)	5 (18%)
20–	11 (41%)	8 (30%)
30–	7 (26%)	8 (30%)
40–	2 (7%)	2 (7%)
50+	2 (7%)	0

of the small numbers involved, the cases in coalface workers and in workmen employed elsewhere underground have been combined for each colliery. The most striking feature is the long period at work which usually preceded the development of dermatitis. Eighty-one per cent (" high claim " colliery) and 67% (" low claim " colliery) were exposed for 20 years or more before the first appearance of the disease. For all miners affected the mean duration of employment was 27 and 24 years respectively in the two collieries, a latent period which is greater than the average of 15 years (in 59 colliery workers) reported by Sneddon (1951).

Chronicity and Incapacity.—The duration of the present attack, as measured at the time of examination, is shown in Table 7. The results illustrate the considerable chronicity of occupational dermatitis; in both collieries 40% of cases had persisted for more than 12 months. Cases of short duration are few. It may be concluded that equally in the two collieries the disease was generally persistent and often protracted.

TABLE 7

DURATION OF PRESENT ATTACK OF OCCUPATIONAL DERMATITIS

Duration	" High Claim " Colliery	" Low Claim " Colliery
	No.	No.
Less than 1 month	3 (11%)	1 (4%)
1–3 months	3 (11%)	4 (15%)
3–6 months	6 (22%)	3 (11%)
6–9 months	1 (4%)	6 (22%)
9–12 months	3 (11%)	2 (7%)
1–2 years	4 (15%)	5 (19%)
2–5 years	4 (15%)	2 (7%)
5+years	3 (11%)	4 (15%)

It must be stressed that most cases were studied at a single interview. Therefore, in the absence of a follow-up examination it was often difficult to assess the severity of the present attack on clinical grounds alone. As the present attack was often a repetition of a past attack, an alternative method of measuring the severity was obtained by combining the loss of work resulting from all attacks. Table 8 contrasts the total absence from work sustained by the two groups of workmen in past and present attacks of occupational dermatitis. The following differences in

TABLE 8

TOTAL ABSENCE FROM WORK ON ACCOUNT OF PAST AND PRESENT OCCUPATIONAL DERMATITIS

Duration of Absence	" High Claim " Colliery	" Low Claim " Colliery
	No.	No.
Nil	7 (26%)	14 (52%)
Less than 1 month	3 (11%)	6 (22%)
1–3 months	6 (22%)	1 (3%)
3–6 months	3 (11%)	3 (11%)
6–12 months	5 (19%)	1 (4%)
1–2 years	1 (4%)	1 (4%)
2+years	2 (7%)	1 (4%)

the record of absence are apparent. (1) Attendance at work was more frequently interrupted among the miners with occupational dermatitis in " high claim " colliery, where working time was lost in 74% of cases compared with 48% in " low claim " colliery. (2) The frequency with which serious loss of work was sustained was also greater in " high claim " colliery, 30% of those affected losing more than six months, compared with the corresponding figure of 12% in " low claim " colliery. These differences reflect the tendency for more severe occupational dermatitis to occur among the miners in " high claim " colliery.

Further support for this observation is given by comparing the dermatitis certification rates in the two groups of workmen for the five-year period preceding the surveys. Thus 19 of the 27 miners with occupational dermatitis in " high claim " colliery were granted compensation, and together these workmen accounted for a total of 46 separate certifications. In " low claim " colliery, on the other hand, seven out of the 27 miners affected were compensated, and the total number of certifications among them was 19.

Non-occupational Dermatitis.—Table 9 shows the prevalence of non-occupational dermatitis among the populations surveyed. Hypostatic eczema was inevitably aggravated by trauma at work; in one case local injury initiated the condition. Foot powders and antihistamine cream accounted for four cases of contact sensitization dermatitis; penicillin tulle was incriminated in a further case, while

TABLE 9

PREVALENCE OF NON-OCCUPATIONAL DERMATITIS IN POPULATIONS SURVEYED ACCORDING TO CLINICAL TYPE

Colliery	" High Claim " (Pop. surveyed, 1,014)	" Low Claim " (Pop. surveyed, 1,073)
Clinical Type	No.	No.
Hypostatic eczema	7 (0·7%)	4 (0·3%)
Besnier's prurigo	2	2
Contact sensitization dermatitis	2	4
Seborrhoeic dermatitis	6 (0·6%)	9 (0·8%)
Infective eczema	2	1
Pompholyx of hands and feet	1	1
Total.. ..	20 (2·0%)	21 (2·0%)

sensitization to nickel was the probable cause in an official who kept a small metal tape measure in his trouser pocket. Infective eczema consisted in each case of unilateral otitis externa with local eczematization of the pinna and cheek.

Dermatitis Possibly Related to Occupation.—While the aetiology of the cases in this group could not be established, it was possible that occupational factors played a contributory part in their causation. Compared with occupational dermatitis they differed in that the history was short and the dermatitis localized to one place on the body. From a study of the cases two main observations were made:

Relationship with Occupation.—Table 10 shows the prevalence of the localized type of dermatitis in which the cause was uncertain in the surface and below ground workers at the two collieries. The prevalence among the surface workers was more than three times the rate in the workers below ground. No satisfactory reason to account for this marked difference could be found, but it may be significant that, of the total surface workmen affected, seven had previously worked below ground.

Absence from Work.—Compared with the occupational dermatitis group, this type of dermatitis caused little loss of work. Though the duration was never greater than two months, seven of the miners affected in " high claim " colliery compared with three in " low claim " colliery lost work. This difference, while smaller than that observed among the cases of occupational dermatitis, is similarly correlated with a higher rate of dermatitis certification in " high claim " colliery, where six out of the 22 cases had received compensation in the past compared with two of the 23 in " low claim " colliery.

TABLE 10

PREVALENCE OF LOCALIZED DERMATITIS, POSSIBLY OCCUPATIONAL, IN SURFACE AND BELOW GROUND WORKERS EXAMINED

Colliery	Surface Workers		Below Ground Workers		Total	
	No. Examined	No. of Cases	No. Examined	No. of Cases	No. Examined	No. of Cases
" High claim "	207	12 (5·8%)	807	10 (1·2%)	1,014	22 (2·2%)
" Low claim "	172	9 (5·2%)	901	14 (1·6%)	1,073	23 (2·1%)

Discussion

This work demonstrated that by the use of suitable methods it is possible to examine for evidence of skin disease the entire population of a colliery, a result which made possible the accurate measurement of the amount of dermatitis at the time of the survey. That this was achieved at both collieries is important, since the main objective was to compare the actual prevalence of dermatitis in each of the two populations.

As regards the results, the most important finding is the close similarity of the prevalence of dermatitis in the two collieries. This is quite unlike the outcome expected from examining the claims for dermatitis compensation, and it can be concluded that in the two collieries the rate at which claims were lodged does not reflect the real prevalence of the disease. The higher rate among the miners in " high claim " colliery is explained by the observation that the cases of occupational dermatitis were more severe than those in " low claim " colliery. As a result loss of work was more common, and as a claim for benefit was usually made at the beginning of each period of unemployment, the number of claims was correspondingly greater. There is an alternative explanation for the observed disparity between prevalence and claims which might apply to both collieries but more particularly to " high claim " colliery where the difference is greatest and the disease more severe. It is possible that a first attack or recurrence causes a claimant to leave the mining industry, and in these circumstances the estimates of prevalence as measured in the present investigation would be less than those based on claims for compensation. That this explanation, however, applies to neither colliery is shown by the fact that not a single instance was recorded where a claimant left the industry as the result of dermatitis, either during the surveys or, so far as could be ascertained from the colliery medical records, during the 18-month period preceding the surveys.

From the point of view of investigating the causes

of occupational dermatitis, the results are less striking; the number of cases for detailed study was small in both colliery surveys. The most significant clue is the tendency for the rash to be localized on the lower limbs, particularly in the region of the ankles, and on the dorsa of the feet. It suggests that mechanical trauma is the main factor responsible. This conclusion is supported by the observation that in the two broad occupational groups working below ground the frequency with which the lower limbs are involved is greatest among those most exposed to trauma, namely, in workers at the coal-face.

Frictional damage is the chief type of mechanical injury to which the skin is subjected in the mining industry. In faceworkers frictional damage can arise either from dust particles which collect in the boot top, and impregnate the socks and trousers, or from constant rubbing together of apposed surfaces through habitual kneeling or squatting at work. The manifestations of continued frictional wear and tear are not immediately obvious; a latent period of the order of 20 years precedes the first appearance of dermatitis. What determines the final breakdown of the skin and the development of the disease is as yet unknown. Repeated frictional damage is but one factor among several in the aetiology of miner's dermatitis, and in the present investigation it was not possible to examine the role of constitutional and psychological factors. The purely provocative role of an exogenous factor such as frictional damage is, however, emphasized by the relative infrequency with which miners develop dermatitis before they have been employed for at least 15 years. Constitutional factors, as yet poorly understood, determine the development and course of the disease. In the ageing miner, for example, vascular responsiveness and cell metabolism may be so altered that in the face of continued frictional wear and tear the skin surrenders to dermatitis.

The natural history of miner's dermatitis as illustrated by the cases studied in this report can be summarized as follows. It is a disease of moderately high prevalence which affects workmen in the fifth and sixth decades after 20 years or more of work below ground. It is characterized by a predilection for the lower limbs, and is primarily determined by mechanical trauma. While generally persistent and often protracted, the severity is variable.

I am grateful to Dr. Geoffrey Hodgson for his help and guidance, and I should like to record my gratitude to the management and men, and the nursing officers, of the two collieries. Without their cooperation this investigation would not have been possible.

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ACCIDENTS IN A NAVAL DOCKYARD

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The high incidence of accidents in H.M. Dockyard, Singapore, during 1954 led to a more detailed recording and analysis in 1955-56. The departmental accident rates per 1,000 workers were recorded, together with the circumstances of all injuries resulting in the loss of more than one shift (two per working day, lasting four and a half hours in the mornings and three and three-quarter hours in the afternoons).

In the successive quarters of 1955, the numbers of accidents of all degrees of severity dropped steadily, but by 1956 they had levelled out at figures ranging from one-sixth to one-quarter of the original numbers. In 1956 the numbers of minor accidents reported were 44% of those for 1955, while cases requiring hospital treatment had fallen to 53·5%. This was balanced to some extent by an increase of trivial cases treated without loss of time by first aid in the workshops, but the total numbers still showed a reduction in the accident rate per 1,000 workers of 26·2%.

Recording every possible form of accident for the year 1955, a rate of 2·38 accidents per 100 employee-months was obtained which differs markedly from rates published for industrial workers in Britain.

The ethnic groups employed all showed a similar decrease in accident rates, but the reduction was noticeably greater among the Malays than the Chinese or Indians.

Analysis by category of causation showed that the lower incidence was largely due to improvement in the categories of handling stores, using hand tools and power-driven machinery, but attention to the causes of eye injuries occasioned a reduction of only 5·2%.

Analysis of time lost showed that the improvement in 1956 was due mainly to two groups. The number of persons experiencing accidents resulting in the loss of two shifts dropped to one-quarter of those found in 1955, while those losing seven shifts, who would in Britain require notification under the Factories Act, 1937, showed a reduction of exactly one-third.

Accident rates were highest in Chinese and Indians between 26 and 35 years of age, but in Malays in the subsequent decade.

In the Island of Singapore there is established one of H.M. dockyards of a size capable of dealing with any class of ship. Some 10,000 persons belonging to several different ethnic groups are employed in the dockyard, but of these a number are listed as "non-industrial", or are employed on work that is unlikely to bring them into contact with industrial hazards. The remainder, 7,122 males, an average figure over the years 1955-56, were on the books of the eight departments principally concerned with industrial work. This number was made up of 2,298 Chinese, 3,680 Indians, 1,133 Malays, and 11 Eurasians.

About 250 women were also employed, but no accidents were reported among them during 1955-56.

At the end of 1954, the number of accidents in the dockyard was considered greater than was justifiable. The recording of accidents was also inaccurate and the degree of severity was not noted. A new routine was therefore instituted, so that race, age, department, and cause for each accident and whether it was necessary to send the patient to hospital for further treatment or investigation were recorded.

Accidents fell into three degrees of severity:

(1) The very trivial, in which the employee was treated on the spot from the first aid box.

(2) Those cases seen by the foreman and sent for treatment to the dockyard dressing stations. There were two of these stations, centrally sited and no man had to walk more than half a mile. Cases reporting at the dressing stations with injuries

incurred on duty were accepted as accidents for the purpose of this study.

(3) Cases seen in the dressing stations by the senior surgery assistant or the hospital assistants and considered to need further examination or treatment in the R.N. Asian hospital, to which they were sent. These were subsequently listed as hospital (H) cases.

It is possible that some variation in degree of severity may have existed in cases transferred to the dressing stations or hospital. Some foremen or hospital assistants may have tended to send men with minor injuries for treatment elsewhere while others dealt with them locally and returned them to duty. No marked variation in the degree of injury of cases reporting was, however, attributable to this cause.

Beginning in 1955, at the end of each month, a nominal roll of all H cases was sent to the respective departments to aid them in pinpointing areas where most accidents were occurring. At the end of each quarter a general analysis of accidents was issued under the various categories of causation, and placing the departments in descending order of the rates of accidents occurring per 1,000 workers.

An immediate reaction was observed. The heads of most departments discussed the list of accidents with their foremen and inspectors and demanded immediate action. It became a point of honour not to head the list with the highest rate, and until the accuracy of the numbers given had been proved in detail over the first few months, attempts to combat or deny the figures were made by several departments. When it was at length realized that this was no attempt to pillory any particular section, but merely to assist in the reduction of man hours lost through unnecessary accidents, cooperation became general.

The effect of greater watchfulness in supervision and possibly the increase in awareness generated among the workers was shown by a remarkable drop in the number of accidents, which continued throughout 1955. The total for the fourth quarter of 1955 was the lowest experienced, and was actually less than in any quarter of 1956. By 1956, however, the quarterly number of accidents was apparently stabilized at a figure approximately one-fourth of that of the first quarter of 1955. The numbers of accidents occurring are shown in Table 1.

Over the two years a considerable increase occurred in the number of cases treated in the departments. While these were of too minor a degree to be included in the official figures, undoubtedly some of the simpler cases formerly attending the dressing stations were treated from the first aid box in the departments.

In 1955, 1,794 accidents were reported, but in the following year the total had dropped to 805, or 44·0% of the former figure. Cases sent to hospital showed a reduction to 53·5%. The individual ethnic groups showed similar reductions in number of accidents.

Fig. 1 gives the quarterly accident rates (expressed as annual rates) and annual rates, in ethnic groups, for the two years studied. In the first quarter, the Malays had far the highest record, with the Chinese next and the Indians lowest. But by the second quarter, the rates were already approximating, and in the third, Malay and Indian were almost identical. Thereafter the Malay showed a lower rate than either Chinese or Indian.

The rapid fall in accident rates during 1955 is most striking. By 1956, the number of accidents did not vary greatly from quarter to quarter.

The possibility that the rates for the three ethnic groups were affected by differences in exposure to accident or in distances from the sick bay was examined. The Chinese had a relative excess in

TABLE 1

ANNUAL AND QUARTERLY NUMBERS OF ACCIDENTS AT H.M. DOCKYARD, SINGAPORE, IN 1955 AND 1956 IN MALE INDUSTRIAL WORKERS CLASSIFIED BY ETHNIC GROUPS

Year	Ethnic Group	Average Population in Year	Quarterly No. of Accidents				Annual Total No. of Accidents	Accident Rate per 1,000 Workers per Annum
			1st	2nd	3rd	4th		
1955	Chinese	2,330	307	145	133	47	632	260·5
	Indian	3,718	372	220	153	75	820	211·4
	Malays	1,141	194	76	47	20	337	294·6
	Eurasians	11	1	1	1	2	5	(—)
	All workers	7,200	874	442	334	144	1,794	249·2
	H cases*	—	181	160	83	62	486	67·5
1956	Chinese	2,266	78	69	57	68	272	120·0
	Indian	3,641	88	106	138	109	441	121·1
	Malays	1,125	26	13	27	24	90	80·0
	Eruasians	11	—	—	—	2	2	(—)
	All workers	7,043	192	188	222	203	805	114·3
	H cases*	—	65	68	59	68	260	36·9

*H cases are those sent to the R.N. Asian hospital for further treatment.

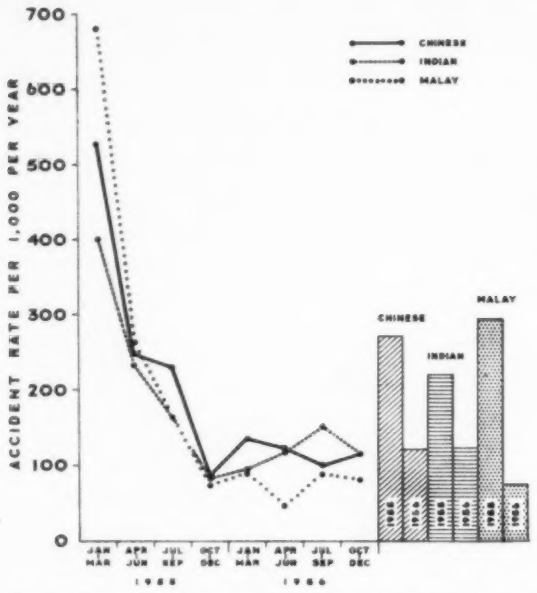

FIG. 1.—Quarterly accident rates (expressed as annual rates)i n ethnic groups.

the departments of the constructor and engineer, the Indians in that of the civil engineer, and the Malays in the Armament Supply Depot. It is unlikely that the last two would have had any marked effect on the total number of accidents, but the concentration of 1,031 Chinese in the skilled artisan grade of the first two departments, whose accident rates were amongst the highest found, might be expected to increase the rate for this ethnic group. The distances of the various departments from the dressing stations were approximately the same and no difference in accident rates between the ethnic groups could be attributed to this factor.

Cases treated in their own departments numbered 265 in 1955 and 682 in 1956. If these were included with those reporting to the dressing stations, accidents in 1955 and 1956 would number respectively 2,059 and 1,487, giving annual rates of 286·0 and 211·1. Though by no means so marked, this still represents a substantial reduction. The reduction in the number of cases sent to hospital from 486 in 1955 to 260 in 1956 is striking.

The accident rate per 100 employee-months can be calculated from Table 1. This index was chosen as the most convenient by Sutherland, Harris, and Smithers (1950) who reported 14·5 accidents per 100 employee-months in an assembly factory and 49·4 in a light engineering factory. In the Singapore dockyard equivalent rates for the Chinese in 1956 were 1·00, for the Indians 1·01, and for the Malays 0·67. The differences between these and Sutherland's figures are enormous and difficult to explain. Sutherland recorded every accident however trivial, and it is possible that first aid in the British factories was obtainable at a shorter distance, more easily, and possibly in a more welcoming environment. Vernon (1936) reported nearly two minor accidents a year per man employed at the Stanton Ironworks between 1927 and 1932, and at three other large works, the character of which was not stated, in one year 9,000 workers suffered 563 reportable accidents and 41,160 accidents requiring first aid. These figures approach an average of five accidents a man each year or 41·7 accidents per 100 employee-months. Even if the very minor accidents at Singapore are included, the accident rates for 1955 and 1956 for all industrial workers become only 2·38 and 1·76 respectively per 100 employee-months. Nor is this due to a weighting of the rates by a majority of the workers being engaged in less dangerous jobs. The work of a dockyard embraces most forms of industrial activity and the largest departments are those of construction (repair and alterations to ships) and of engineering.

The highest rate for 1956 was produced by the department of victualling stores, which, with 79 male workers, gave a rate of 253·2 per 1,000 workers. If the 30 trivial cases treated in the department itself are added, the rate rises to 633·6 per 1,000 workers, equivalent to 5·28 accidents per 100 employee-months. In 1955 this department, with 75 accidents recorded in the dressing station and 12 treated in the department, gave a total rate of 1,035·7 per 1,000 male employees or 8·63 accidents per 100 employee-months. The highest departmental accident rate in the Singapore dockyard was thus much below the rates recorded by Sutherland for British factories. This difference may be associated with a greater tendency to report accidents in Britain.

Categories of Causation

Table 2 gives the numbers of accidents occurring in 1955 and 1956, separated into 11 categories of causation. For each category the rate per 1,000 workers is shown, and the percentage reduction between the two years.

The accidents in the categories of handling stores, using hand tools, using power-driven machinery, burns and scalds, and electrical accidents were all reduced by approximately 70 to 80%, eye injuries were lessened by only 5·2%, struck by falling objects by 11·1%, and persons falling by 25·3%. The reduction in accidents which occurred in 1956 was due mainly to the improvement in the first three of these categories. Furthermore, the last three categories together were only reduced by 71 accidents and in 1956 they constituted 52·3% of all accidents.

TABLE 2

NUMBERS OF ACCIDENTS AND RATE PER 1,000 WORKERS IN 11 CATEGORIES OF CAUSATION IN SINGAPORE DOCKYARD IN 1955 AND 1956

Year	No. Employed		Category of Causation											Total
			Handling Stores	Persons Falling	Struck by Falling Objects	Stepping on or Striking Objects	Using Hand Tools	Using Power-driven Machinery	Burns and Scalds	Welding	Transport	Electrical	Eye Injury on Duty	
1955	7,200	No. of accidents	307	140	143	170	320	258	94	43	75	35	209	1,794
		Rate per 1,000 workers	42·6	19·4	19·9	23·6	44·4	35·8	13·1	6·0	10·4	4·9	29·0	249·2
1956	7,043	No. of accidents	70	102	125	79	88	58	31	22	30	6	194	805
		Rate per 1,000 workers	9·9	14·5	17·7	11·2	12·5	8·2	4·4	3·1	4·3	·9	27·5	114·3
The accident rate for 1956 expressed as a percentage of that for 1955			23·2	74·7	88·9	47·5	28·2	22·9	33·6	51·7	41·3	18·4	94·8	44·9

These are evidently the groups which require closer supervision and an increase of safety instruction among the workers. The National Safety Council of U.S. (1952) reported that, in the United States, 22% of all industrial accidents were caused during handling stores, 17% by falls, and 16% by machinery. Taylor (1954) gives 27%, 14%, and 16% respectively in these categories. In the Singapore dockyard the corresponding percentages were 17·1, 7·8, and 14·4 in 1955 and 8·7, 12·6, and 7·2 in 1956. The Singapore 1955 percentages of accidents caused by handling stores and machinery were of the same order as those given by the National Safety Council of U.S. and Taylor; in 1956, however, there was a considerable reduction in the percentage of accidents due to handling stores and machinery, with a relative increase in those due to falls.

The accident rates in 1956 varied considerably between the various departments of the dockyard. In several instances unexpected results were found. In four departments (construction, engineering, civil engineering, and naval stores) the number of eye accidents increased in 1956; accidents from falling and being struck by falling objects also increased in two departments. Although the total number of accidents in all departments was greatly reduced, these results indicate danger points for further accident prevention.

Loss of Working Times in Cases Sent to Hospital

In H.M. Dockyard, Singapore, the working day is divided into two shifts, 7 a.m. to 11.30 a.m. and 12.45 to 4.15 p.m. The severity of an accident was measured roughly by the number of shifts lost before the employee returned to work.

The total number of accident cases referred to hospital in the two years 1955 and 1956 was 746 and none of these patients returned to duty with the loss of less than two shifts. Table 3, for cases referred to hospital, gives the numbers of workers losing two, three, or more shifts as a result of their injury. Those absent from work for seven or more shifts, who in Britain would require notification under the Factories Act of 1937 as experiencing accidents where more than three working days were lost, are included in one group.

TABLE 3

NO. OF SHIFTS LOST IN ACCIDENT CASES REFERRED TO HOSPITAL AND INTERNATIONAL FREQUENCY RATE AT SINGAPORE DOCKYARD 1955 AND 1956

Year	No. of Workers Referred to Hospital after Accident: Shifts Lost						Total	International Frequency Rate, *i.e.*, No. of Accidents Causing Loss of Working Time per 100,000 Man-hours Worked
	2	3	4	5	6	7+		
1955	264	41	17	25	43	96	486	3·2
1956	67	33	25	27	44	64	260	1·7
H accidents in 1956 as a percentage of those in 1955	25·4	80·5	147·1	108·0	102·3	66·6	53·5	

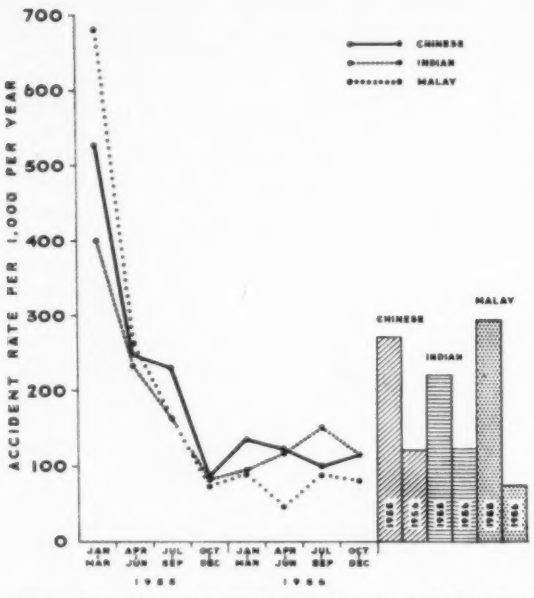

FIG. 1.—Quarterly accident rates (expressed as annual rates)i n ethnic groups.

the departments of the constructor and engineer, the Indians in that of the civil engineer, and the Malays in the Armament Supply Depot. It is unlikely that the last two would have had any marked effect on the total number of accidents, but the concentration of 1,031 Chinese in the skilled artisan grade of the first two departments, whose accident rates were amongst the highest found, might be expected to increase the rate for this ethnic group. The distances of the various departments from the dressing stations were approximately the same and no difference in accident rates between the ethnic groups could be attributed to this factor.

Cases treated in their own departments numbered 265 in 1955 and 682 in 1956. If these were included with those reporting to the dressing stations, accidents in 1955 and 1956 would number respectively 2,059 and 1,487, giving annual rates of 286·0 and 211·1. Though by no means so marked, this still represents a substantial reduction. The reduction in the number of cases sent to hospital from 486 in 1955 to 260 in 1956 is striking.

The accident rate per 100 employee-months can be calculated from Table 1. This index was chosen as the most convenient by Sutherland, Harris, and Smithers (1950) who reported 14·5 accidents per 100 employee-months in an assembly factory and 49·4 in a light engineering factory. In the Singapore dockyard equivalent rates for the Chinese in 1956 were 1·00, for the Indians 1·01, and for the Malays 0·67. The differences between these and Sutherland's figures are enormous and difficult to explain. Sutherland recorded every accident however trivial, and it is possible that first aid in the British factories was obtainable at a shorter distance, more easily, and possibly in a more welcoming environment. Vernon (1936) reported nearly two minor accidents a year per man employed at the Stanton Ironworks between 1927 and 1932, and at three other large works, the character of which was not stated, in one year 9,000 workers suffered 563 reportable accidents and 41,160 accidents requiring first aid. These figures approach an average of five accidents a man each year or 41·7 accidents per 100 employee-months. Even if the very minor accidents at Singapore are included, the accident rates for 1955 and 1956 for all industrial workers become only 2·38 and 1·76 respectively per 100 employee-months. Nor is this due to a weighting of the rates by a majority of the workers being engaged in less dangerous jobs. The work of a dockyard embraces most forms of industrial activity and the largest departments are those of construction (repair and alterations to ships) and of engineering.

The highest rate for 1956 was produced by the department of victualling stores, which, with 79 male workers, gave a rate of 253·2 per 1,000 workers. If the 30 trivial cases treated in the department itself are added, the rate rises to 633·6 per 1,000 workers, equivalent to 5·28 accidents per 100 employee-months. In 1955 this department, with 75 accidents recorded in the dressing station and 12 treated in the department, gave a total rate of 1,035·7 per 1,000 male employees or 8·63 accidents per 100 employee-months. The highest departmental accident rate in the Singapore dockyard was thus much below the rates recorded by Sutherland for British factories. This difference may be associated with a greater tendency to report accidents in Britain.

Categories of Causation

Table 2 gives the numbers of accidents occurring in 1955 and 1956, separated into 11 categories of causation. For each category the rate per 1,000 workers is shown, and the percentage reduction between the two years.

The accidents in the categories of handling stores, using hand tools, using power-driven machinery, burns and scalds, and electrical accidents were all reduced by approximately 70 to 80%, eye injuries were lessened by only 5·2%, struck by falling objects by 11·1%, and persons falling by 25·3%. The reduction in accidents which occurred in 1956 was due mainly to the improvement in the first three of these categories. Furthermore, the last three categories together were only reduced by 71 accidents and in 1956 they constituted 52·3% of all accidents.

TABLE 2

NUMBERS OF ACCIDENTS AND RATE PER 1,000 WORKERS IN 11 CATEGORIES OF CAUSATION IN SINGAPORE DOCKYARD IN 1955 AND 1956

Year	No. Employed		Category of Causation											Total
			Handling Stores	Persons Falling	Struck by Falling Objects	Stepping on or Striking Objects	Using Hand Tools	Using Power-driven Machinery	Burns and Scalds	Welding	Transport	Electrical	Eye Injury on Duty	
1955	7,200	No. of accidents	307	140	143	170	320	258	94	43	75	35	209	1,794
		Rate per 1,000 workers	42·6	19·4	19·9	23·6	44·4	35·8	13·1	6·0	10·4	4·9	29·0	249·2
1956	7,043	No. of accidents	70	102	125	79	88	58	31	22	30	6	194	805
		Rate per 1,000 workers	9·9	14·5	17·7	11·2	12·5	8·2	4·4	3·1	4·3	·9	27·5	114·3
The accident rate for 1956 expressed as a percentage of that for 1955			23·2	74·7	88·9	47·5	28·2	22·9	33·6	51·7	41·3	18·4	94·8	44·9

These are evidently the groups which require closer supervision and an increase of safety instruction among the workers. The National Safety Council of U.S. (1952) reported that, in the United States, 22% of all industrial accidents were caused during handling stores, 17% by falls, and 16% by machinery. Taylor (1954) gives 27%, 14%, and 16% respectively in these categories. In the Singapore dockyard the corresponding percentages were 17·1, 7·8, and 14·4 in 1955 and 8·7, 12·6, and 7·2 in 1956. The Singapore 1955 percentages of accidents caused by handling stores and machinery were of the same order as those given by the National Safety Council of U.S. and Taylor; in 1956, however, there was a considerable reduction in the percentage of accidents due to handling stores and machinery, with a relative increase in those due to falls.

The accident rates in 1956 varied considerably between the various departments of the dockyard. In several instances unexpected results were found. In four departments (construction, engineering, civil engineering, and naval stores) the number of eye accidents increased in 1956; accidents from falling and being struck by falling objects also increased in two departments. Although the total number of accidents in all departments was greatly reduced, these results indicate danger points for further accident prevention.

Loss of Working Times in Cases Sent to Hospital

In H.M. Dockyard, Singapore, the working day is divided into two shifts, 7 a.m. to 11.30 a.m. and 12.45 to 4.15 p.m. The severity of an accident was measured roughly by the number of shifts lost before the employee returned to work.

The total number of accident cases referred to hospital in the two years 1955 and 1956 was 746 and none of these patients returned to duty with the loss of less than two shifts. Table 3, for cases referred to hospital, gives the numbers of workers losing two, three, or more shifts as a result of their injury. Those absent from work for seven or more shifts, who in Britain would require notification under the Factories Act of 1937 as experiencing accidents where more than three working days were lost, are included in one group.

TABLE 3

NO. OF SHIFTS LOST IN ACCIDENT CASES REFERRED TO HOSPITAL AND INTERNATIONAL FREQUENCY RATE AT SINGAPORE DOCKYARD 1955 AND 1956

Year	No. of Workers Referred to Hospital after Accident: Shifts Lost						Total	International Frequency Rate, *i.e.*, No. of Accidents Causing Loss of Working Time per 100,000 Man-hours Worked
	2	3	4	5	6	7+		
1955	264	41	17	25	43	96	486	3·2
1956	67	33	25	27	44	64	260	1·7
H accidents in 1956 as a percentage of those in 1955	25·4	80·5	147·1	108·0	102·3	66·6	53·5	

TABLE 4

NO. OF ACCIDENT CASES REFERRED TO HOSPITAL FROM H.M. DOCKYARD, SINGAPORE, IN 1955 AND 1956, LIABLE TO NOTIFICATION UNDER FACTORIES ACT, 1937, AND PERCENTAGE IN EACH CATEGORY OF CAUSATION COMPARED WITH UNITED KINGDOM PERCENTAGE

Causation Category of Accident	No. of Accident Cases Referred to Hospital			% of Total	% of Total United Kingdom Reportable Accidents in Each Category (H.M. Chief Inspector, 1955)
	1955	1956	Total		
Handling goods or stores	15	2	17	10·6	27·3
Persons falling	7	9	16	10·0	13·9
Struck by falling bodies	13	11	24	15·0	8·4
Stepping on or striking objects	3	5	8	5·0	8·2
Using hand tools	16	8	24	15·8	8·0
Using power-driven machinery	14	10	24	15·0	15·8
Transport	2	2	4	2·5	5·7
Burns and scalds	3	1	4	2·5	
Welding	1	—	1	·6	12·7
Electrical	1	—	1	·6	
Eye injuries	21	16	37	23·1	
Total:	96	64	160	100·7	100·0

With the exception of the accidents involving the loss of seven shifts or more, which were reduced by one-third, the greatest saving in time lost was for the accidents in which two shifts were lost. These fell in 1956 to a quarter of the number recorded in 1955.

There were 96 accidents resulting in the loss of seven shifts or more in 1955 and 64 in 1956. The rates of accidents which would have been notifiable under the Factories Act per 1,000 workers were 13.3 in 1955 and 9·1 in 1956. H.M. Chief Inspector of Factories (1955) gives a corresponding rate for the United Kingdom of about 24, which is considerably higher. The numbers and percentages of accident cases occurring in the various causation categories in Britain and in Singapore Dockyard are compared in Table 4 for the accidents resulting in more than three days' absence from work.

It will be seen that the percentages due to handling stores or goods are much lower in Singapore than those under equivalent categories in the United Kingdom, but those under "struck by falling objects", using hand tools, and eye injuries are greater. Vernon (1936) quotes the 1928 and 1932 reports of the Chief Inspector of Factories to show that eye injuries incurred in industry averaged 4·3% and 4·2% respectively of all reportable accidents, and also that the highest percentage in any one year was 8·3%. The percentage of eye injuries over two years in Singapore amounted to nearly three times the highest percentage recorded in the United Kingdom, but of course, percentage distribution in any one category may fluctuate with changes in other categories.

Accidents as Affected by Age and Ethnic Group

Workers in H.M. Dockyard, Singapore, are of all ages from 16 to a maximum of 65. As in other parts of this study, the term "accident" includes all cases referred to the dockyard dressing stations or to hospital. The annual average number of accidents occurring during 1955 and 1956 was calculated, and the rates for three ethnic groups in 10-year age groups are shown in Fig. 2 and Table 5.

In Table 6, the annual average numbers of accidents are subdivided by ethnic group and category of causation.

Among Chinese and Indians the accident rate increases to a peak in the second age group and falls steadily away thereafter; in the Malays the peak occurs in the 36 to 45 age group. In the veterans of 56 years and more the rate is notably low for Chinese and Malays. These rates, based on an average of two years with very different accident records, are of course misleading in themselves but portray accurately the relation between the age groups.

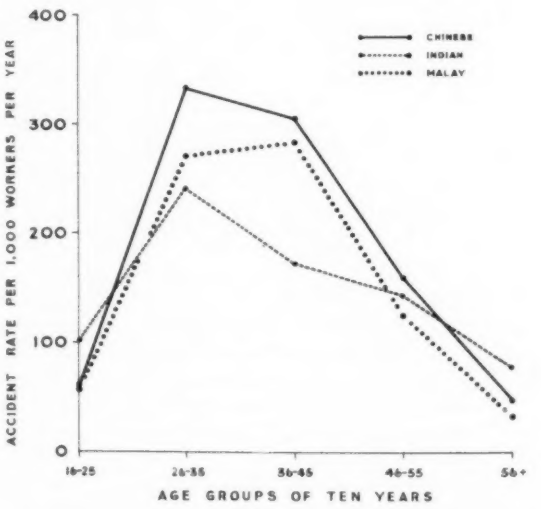

FIG. 2.—Accident rates for the three ethnic groups in 10-year age groups.

TABLE 5

ANNUAL AVERAGE NO. OF ACCIDENTS IN MALE INDUSTRIAL WORKERS IN H.M. DOCKYARD, SINGAPORE, IN 1955 AND 1956 AND RATES PER 1,000 WORKERS IN AGE AND ETHNIC GROUPS

Ethnic Group		Age Group					All Ages
		16-25	26-35	36-45	46-55	56 +	
Chinese	Average no. in group	695	603	431	368	200	2,297
	Average no. of accidents per annum	42·5	199·5	135·0	57·5	9·5	444·0
	Annual rate per 1,000 workers	61·2	330·8	313·3	156·2	47·5	193·3
Indian	Average no. in group	620	1,175	1,242	517	125	3,679
	Average no. of accidents per annum	64·5	282·5	212·0	74·0	10·0	643·0
	Annual rate per 1,000 workers	104·0	240·0	170·0	143·1	80·0	174·8
Malay	Average no. in group	358	377	213	139	45	1,132
	Average no. of accidents per annum	21·0	112·5	61·5	17·5	1·5	214·0
	Annual rate per 1,000 workers	58·7	271·9	288·7	125·9	33·3	189·0

TABLE 6

ANNUAL AVERAGE NUMBER OF ACCIDENTS IN MALE INDUSTRIAL WORKERS OF H.M. DOCKYARD, SINGAPORE IN 1955 AND 1956 AND RATES PER 1,000 WORKERS IN ETHNIC GROUPS AND CATEGORIES OF CAUSATION

Ethnic Group	Annual Average No. in Group		Handling Stores	Persons Falling	Struck by Falling Objects	Stepping on or Striking Objects	Using Hand Tools	Using Power-driven Machinery	Burns and Scalds	Welding	Transport	Electrical	Eye Injuries	All Accidents
Chinese	2,297	Average no. of accidents per annum	74·0	33·5	46·0	38·5	62·5	57·5	24·5	11·5	18·0	11·5	66·5	444·0
		Per cent of all accidents	16·9	7·6	10·5	8·8	14·2	13·1	5·6	2·6	4·1	1·5	15·1	100·0
		Annual rate per 1,000 workers	32·2	14·6	20·0	16·8	27·2	25·0	10·7	5·0	7·8	2·7	29·0	193·3
Indian	3,679	Average no. of accidents per annum	61·5	69·5	76·0	71·5	115·0	63·5	31·5	18·0	20·5	12·5	103·5	643·0
		Per cent of all accidents	9·6	10·8	11·8	11·1	17·9	9·9	4·9	2·8	3·2	1·9	16·1	100·0
		Annual rate per 1,000 workers	16·7	18·9	20·7	19·4	31·3	17·3	8·6	4·9	5·6	3·4	28·1	174·8
Malay	1,132	Average no. of accidents per annum	52·5	17·5	10·5	14·0	26·5	37·0	6·5	3·0	13·5	1·5	31·5	214·0
		Per cent of all accidents	24·5	8·2	4·9	6·5	12·4	17·3	3·0	1·4	6·3	0·7	14·9	99·9
		Annual rate per 1,000 workers	46·4	15·5	9·3	12·4	23·4	32·7	5·7	2·6	11·9	1·3	27·8	189·0

They differ from the findings of Hewes (1921) who, dealing with 2,891 male employees of a Connecticut silk mill, showed that the frequency of accidents was greater under 20 years of age but dwindled steadily thereafter. This was also the experience of Schmitt (1926), but Brundage (1927) showed a comparatively steady frequency rate up to the age of 50 and then a fall.

McFarland (1957) quoted the records of an industrial physician of Ohio, that "50% of industrial accidents occurred in people under the age of 25, and that the rate for the 20-24 year group was more than twice that of the 40-44 age group".

Sutherland *et al.* (1950) show in both groups of factories the highest rates in the youngest age groups decreasing exponentially to a minimum over 55 years of age of between one-third and one-quarter the rates of those under 20.

Kossoris (1948), however, agrees in showing that among 18,000 factory workers the frequency of non-disabling injuries showed a steady decline from the 25 to 27 age group onwards. King and Speakman's suggestion (1953) that the high rate in the younger age groups is largely due to inexperience does not agree with the findings here that those most affected were not the youngest; nor does the very low labour turnover in the dockyard support this suggestion. The other concepts of "general immaturity" and "less responsibility" remain for consideration but must apparently be counterbalanced by carelessness or over-confidence in the middle age groups.

Days and Times of Occurrence of Accidents

In 1956 the accident rates had become stable, and further information was recorded, including the day of the week and the time of the day at which accidents occurred.

TABLE 7

NOS. OF ACCIDENTS OCCURRING ON DIFFERENT DAYS OF THE WEEK AT SINGAPORE DOCKYARD, 1956

Day of Occurence	No. of Accidents	% of Total
Monday	203	25·2
Tuesday	196	24·3
Wednesday	94	11·7
Thursday	84	10·4
Friday	156	19·4
Saturday	61	7·6
Sunday	11	1·4
Total	805	100·0

Table 7 shows the distribution of accidents by day of the week. The accidents included in Table 7 were those in which the employee was sent to a dockyard dressing station or to hospital. During the six weekdays, all employees were present, but on Sundays, as an average, only about 5% were working. On Saturdays one shift was worked in place of the usual two. The accident frequency was highest on Monday and fell to its lowest level at mid-week. This agrees with Factory B of Sutherland *et al.* (1950) for the first three days of the week (476, 466, and 424 accidents) but not for the next two days (481 and 393). Sutherland's Factory A was different on all counts.

Vernon (1918) showed that, with a 12-hour working day, accidents were most frequent on Mondays, sinking to a minimum on Fridays, with an increase once more on Saturdays, and related this to some extent to the consumption of alcohol. This factor would apply very little in Singapore.

The time of day when an accident was sustained was only recorded for cases referred to hospital and the results are shown in Table 8.

The number of accidents rose to a peak between 8 and 10 a.m. and to a lesser ridge between 2 and 3 p.m. Ignoring the few accidents on a Sunday, in the six mornings of four and a half hours each (27 hours) 182 accidents were reported, while in the five afternoons (17½ hours) only 78 occurred. Thus 70% of these accidents took place in the morning at a rate of 6·7 accidents per hour, and 30% in the afternoons at a rate of 4·5 accidents per hour.

Imbert (1904) stated that more accidents occur during the last two hours of the morning and in the afternoon spells of work, but most records of a committee of the British Association (Sargant Florence, 1916) show that accidents increase during the morning to reach a maximum in the last hour or hour but one. In the afternoon the peak period for accidents was around 3 p.m.

Vernon, Bedford, and Warner (1931) also showed that miners attained maximum accident frequency in the last hour of full work at low temperature, but when the temperature was high, accidents reached the peak in the last hour but one. In the Singapore dockyard, where temperatures are high, the second peak of accident frequency was reached in the penultimate hour of afternoon work.

The two factories investigated by Sutherland (1950) differed in their hours of work but the peak periods for accidents were in both instances between 8 and 9 a.m. and 3 and 4 p.m. Sutherland also found that the rate of reporting accidents was from 30 to 40% lower in the afternoon than in the morning.

Conclusions

Accidents occurring to male industrial workers of H.M. Dockyard, Singapore, during the years 1955-56 have been analysed as to age and ethnic group and category of causation. Average numbers employed were 7,200 (1955) and 7,043 (1956).

Cases requiring further investigation or treatment at the R.N. Asian Hospital are shown separately.

The number of accidents reported were 1,794 (1955) and 805 (1956). Expressed as accidents per 100 employee-months this is 1·00 for Chinese, 1·01 for Indians, and 0·67 for Malays.

The rates per 1,000 workers for 1956 for accidents requiring notification under the Factories Act, 1937, is shown as 9·1: the international accident frequency rate is 1·7.

The rates for accidents are highest for Chinese and Indians in the 26 to 35 years of age group, falling to the lowest at 56 years and over. The Malays differ only in having the accident peak in the 36 to 45 age group.

The majority of the accidents occurred on Mondays, falling steadily for the next three days, with a slight secondary peak on Fridays; by far the greatest number occur between 0800 and 1000 every day. During the mornings accidents occur at the rate of 6·7 an hour and in the afternoon at 4·5 an hour (total accidents for the year represented as occurring

TABLE 8

NO. OF ACCIDENTS IN WHICH THE EMPLOYEE WAS REFERRED TO HOSPITAL RELATED TO TIME OF OCCURRENCE AT SINGAPORE DOCKYARD, 1956

	Periods of Working Day							Total No. of Accidents
	0700–	0800–	0900–	1000–	1245–	1400–	1500–1615	
No. of accidents	26	70	63	23	19	43	16	260
No. of accidents per hour	26	70	63	15	15	43	13	—

in one working week).

The types and sites of injuries are tabulated.

I am indebted to Surgeon Vice-Admiral Sir Cyril May, K.B.E., M.C., Medical Director-General of the Navy, for permission to publish this article.

I am also most grateful to Mr. H. H. Dickson, acting senior surgery assistant at H.M. Dockyard, Singapore, for the great assistance he has given in the recording and listing of these accidents.

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THE APRIL (1959) ISSUE

The April (1959) issue contains the following papers:—

Health Problems of Epoxy Resins and Amine-curing Agents. By L. B. Bourne, F. J. M. Milner, and K. B. Alberman.

Medical Examinations for Public Safety. By P. A. B. Raffle.

Measuring Dust Exposure with the Thermal Precipitator in Collieries and Foundries. By S. A. Roach.

Pulmonary Fibrosis in an Aluminium Worker. By John Mitchell.

Two Cases of Hydrazine Hydrate Dermatitis without Systemic Intoxication. By Darrell M. Evans.

The Chemotherapy of Poisoning by Organophosphate Anticholinesterases. By D. R. Davies and A. L. Green.

A Follow-up Study of Men Exposed to Cadmium Oxide Fume. By J. A. Bonnell, G. Kazantzis, and E. King.

The Value of Mobilization of Lead by Calcium Ethylene-diamine-tetra-acetate in the Diagnosis of Lead Poisoning. By J. Teisinger and J. Srbová.

The Mechanical Properties of the Lung in Pneumoconiosis of Coal-miners. By G. L. Leathart.

Further Studies of the Neutralization of Silica Toxicity *In Vitro*. By J. Marks.

Miscellanea:

The Employment of Diabetics. By John F. Copplestone.

Book Reviews.

A number of copies are still available and may be obtained from the Publishing Manager, British Medical Association, Tavistock Square, W.C.1, price 17*s.* 6*d.*

Brit. J. industr. Med., 1959, **16**, 216.

THE ACUTE TOXIC EFFECTS OF BLACK SMOKE

BY

R. E. PATTLE, G. D. WEDD, and F. BURGESS

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(RECEIVED FOR PUBLICATION SEPTEMBER 3, 1958)

Few experiments have been conducted on the toxicity of solid carbonaceous combustion products. In order to obtain an estimate of the toxicity of black smoke which could be compared with similar estimates for other pollutants, the median dosage to death, (Ct)D 50, has been determined for smoke from burning tetrahydronaphthalene administered to guinea-pigs and mice. Values ranging from 147,000 mg. min./m.^{3} to 351,000 mg. min./m.^{3} were obtained at concentrations between 714 mg./m.^{3} and 1,140 mg./m.^{3}. Animals allowed to associate protected one another to some extent, probably owing to their fur acting as a filter.

In mice the cause of death appears to be blockage of the air passages; deaths after removal from the smoke are unusual. In guinea-pigs haemorrhagic lesions are caused, and delayed deaths are commoner.

The action of smoke on rats resembles its action on mice.

It is pointed out that tetralin smoke is considerably more toxic to animals than is sulphur dioxide in the same concentration. This finding is discussed in relation to atmospheric pollution.

Black smoke is an atmospheric pollutant which attracts a good deal of attention. The suspended matter in city air may consist of, say, 1·0 mg./m.^{3} of combustible matter and 0·2 mg./m.^{3} of ash. The combustible matter consists mainly of carbon "tarry matter", *i.e.*, matter insoluble in carbon disulphide, and is present to the extent of 3% to 5% of the suspended solids (Meetham, 1952). The mass median diameter of the particles is of the order 0·5 μ to 1 μ; those particles more than 1 μ across are mainly mineral, and those smaller than this are carbonaceous (Cartwright, Nagelschmidt, and Skidmore, 1956).

Experiments on the toxicity of solid carbonaceous combustion products have been few, and we have found no evidence in the literature of their lethal potentiality. Claisse and Josué (1897) studied anthracosis in animals exposed to unspecified but not lethal dosages of smoke from oil of turpentine (mainly $C_{10}H_{14}$) burning in a lamp. Vintinner and Baetjer (1951) exposed rats to the products of combustion of pulverized coal (mean concentration 57 mg./m.^{3}; maximum dosage 4,200,000 mg. min./m.^{3}). There were no fatalities. The mass median diameter of the particles was probably large, as more than half the aerosol could be removed by filtration through steel wool. Pattle and Burgess (1957) reported exposures of mice to kerosene smoke (354 mg./m.^{3}; dosage 106,200 mg. min./m.^{3}), without fatalities.

It was desired to obtain an estimate of the toxicity of black smoke which could be compared with similar estimates for other pollutants. It was evident that this would require a very high concentration of smoke, such as can conveniently be produced by burning tetralin (tetrahydronaphthalene, $C_{10}H_{12}$). The present work recounts experiments with this smoke; long-term observations on the survivors of these and other experiments are still in progress.

Methods

Production of Tetralin Smoke.—The smoke was produced by burning tetralin in an ordinary hurricane lamp (wick 13 mm. wide) with the glass and upper part removed. It gives a very smoky flame, and has the right flash-point for burning in this type of lamp; the combustion products are not irritant and have a faint smell of naphthalene. The consumption of tetralin was measured by weighing the lamp before and after the experiment; the fraction of the carbon content of the tetralin which was converted to smoke varied from 5% to 11%. The causes of this variation are not clear; it is important as it affects the concentration of smoke which can be obtained without overheating the chamber.

Exposure of Animals to the Smoke.—The animals were contained in cages within a chamber of 110 l. capacity in which the lamp also stood, and 20 or 25 l./min. of air

was blown into the top of the chamber through a tube 6 mm. in diameter; it thus entered with a velocity high enough (1·2 or 1·5 m./sec.) to give adequate stirring, and in quantity sufficient to prevent environmental anoxia. The chamber was opened every 30 min., when the animals were inspected and the relative positions of the cages were changed. The time at which each animal was found dead was noted.

The temperature in the chamber was kept at 29°C. or less by adjusting the wick of the lamp, so that the animals should not suffer from heat stroke. In experiment 4 the incoming air was cooled in ice so that a larger flame could be used without overheating.

In most of the experiments the animals were each kept in a separate small cage or compartment of a larger one, as it was thought that if they were allowed to associate they would protect one another. In some cases, however, a whole batch was placed in one cage. In some experiments the exposure was continued until all the animals in a batch had died; in others, batches were withdrawn while there were still survivors, so that the likelihood of delayed deaths could be assessed and the long-term effects of the exposure could be observed. The details of each experiment are recorded in Table 1.

Sampling the Smoke.—The concentration of the smoke was determined by sampling on a Whatman No. 1 filter paper, using a 1 l./min. critical orifice downstream to control the flow; the paper and deposit did not significantly affect the flow rate. The deposit on the paper was weighed, using a tared filter paper as counterweight. The filter paper was changed every 30 min., but otherwise sampling was continuous; the mean concentration over each half-hour, including the times when the chamber was open for inspection, was thus recorded.

On removal from the chamber and exposure to the air of the balance room the smoke deposit lost about 30% of its weight within two hours. Oven-drying at 90°C. removed another 10%. All the recorded weights were taken after at least two hours' equilibration of the smoke deposit with the room atmosphere.

The content of tarry matter was determined by extracting a known weight of smoke deposit with carbon disulphide and weighing the tar thus obtained.

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To measure this, a batch is exposed to a more or less uniform concentration of a toxic agent, and the time at which each animal dies is noted. From the known concentration the dosage to death, (Ct)D, of each animal is calculated, and the individual (Ct)Ds are treated statistically to obtain a value for the (Ct)D 50 and other data. For the greatest accuracy, the experiment should be continued until all the animals have been killed. If the toxic agent is one which rarely causes delayed deaths, the (Ct)D 50 will be nearly equal to the L(Ct) 50; this is the case with black smoke acting on mice. For agents such as phosgene, which commonly produce delayed death, measurements of the (Ct)D 50 would be of less value.

Statistical Methods of Bliss (1937).—When all the animals in an experiment died, each individual animal was assumed to have died at the geometric mean of the dosages calculated for the last time at which the chamber was opened before, and for the first time it was opened after, the animal died. The logarithms of these dosages were treated as being distributed normally and the mean, its standard error, and the slope of the probit of kill against log. dosage were calculated; the last quantity was corrected for grouping.

After experiments in which several animals died, but left survivors, the probit of kill was plotted against the log. dosage for the time at which each animal was found dead; good straight lines were obtained. From these the log. (Ct)D 50 and slope were read off. The standard error of the log. (Ct)D 50 was calculated by the Bliss formulae, which allow for the increase in error caused by the truncation. The slope was corrected for grouping. No further corrections were applied.

Histological Methods.—Organs were fixed in formol saline and embedded in paraffin wax. Sections were then cut and were stained with haematoxylin and eosin.

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Toxicity of Black Smoke.—The results of four experiments with tetralin smoke are given in Table 1. It will be noted that of 28 deaths in those batches of mice which were withdrawn before they had all died, only one (3·6%) took place after the end of the exposure. In experiment 3, however, of a batch of 10 guinea-pigs which were alive when the exposure was terminated, three died during the subsequent 22 hours.

A number of other exposures of animals to smoke from burning kerosene, from burning coal distillates, and from a diesel engine, have also been carried out. In some of these up to 20 p.p.m. of sulphur dioxide accompanied the smoke. The results have been in accord with those of the experiments recorded in Table 1.

Pathological Findings.—Mice which had died from the acute effects of black smoke showed at necropsy blackening of the lungs, which was especially prominent when a cut surface was viewed. There was no sign of oedema or of widespread atelectasis, but congestion was often marked. The trachea was also blackened and often appeared to be blocked by sooty liquid. Soot was found in the nasal passages and the oesophagus.

Microscopically the absence of oedema was con-

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THE ACUTE TOXIC EFFECTS OF BLACK SMOKE

BY

R. E. PATTLE, G. D. WEDD, and F. BURGESS

From the Chemical Defence Experimental Establishment, Porton Down, Salisbury, Wilts

(RECEIVED FOR PUBLICATION SEPTEMBER 3, 1958)

Few experiments have been conducted on the toxicity of solid carbonaceous combustion products. In order to obtain an estimate of the toxicity of black smoke which could be compared with similar estimates for other pollutants, the median dosage to death, (Ct)D 50, has been determined for smoke from burning tetrahydronaphthalene administered to guinea-pigs and mice. Values ranging from 147,000 mg. min./m.^{3} to 351,000 mg. min./m.^{3} were obtained at concentrations between 714 mg./m.^{3} and 1,140 mg./m.^{3}. Animals allowed to associate protected one another to some extent, probably owing to their fur acting as a filter.

In mice the cause of death appears to be blockage of the air passages; deaths after removal from the smoke are unusual. In guinea-pigs haemorrhagic lesions are caused, and delayed deaths are commoner.

The action of smoke on rats resembles its action on mice.

It is pointed out that tetralin smoke is considerably more toxic to animals than is sulphur dioxide in the same concentration. This finding is discussed in relation to atmospheric pollution.

Black smoke is an atmospheric pollutant which attracts a good deal of attention. The suspended matter in city air may consist of, say, 1·0 mg./m.^{3} of combustible matter and 0·2 mg./m.^{3} of ash. The combustible matter consists mainly of carbon "tarry matter", *i.e.*, matter insoluble in carbon disulphide, and is present to the extent of 3% to 5% of the suspended solids (Meetham, 1952). The mass median diameter of the particles is of the order 0·5 μ to 1 μ; those particles more than 1 μ across are mainly mineral, and those smaller than this are carbonaceous (Cartwright, Nagelschmidt, and Skidmore, 1956).

Experiments on the toxicity of solid carbonaceous combustion products have been few, and we have found no evidence in the literature of their lethal potentiality. Claisse and Josué (1897) studied anthracosis in animals exposed to unspecified but not lethal dosages of smoke from oil of turpentine (mainly $C_{10}H_{16}$) burning in a lamp. Vintinner and Baetjer (1951) exposed rats to the products of combustion of pulverized coal (mean concentration 57 mg./m.^{3}; maximum dosage 4,200,000 mg. min./m.^{3}). There were no fatalities. The mass median diameter of the particles was probably large, as more than half the aerosol could be removed by filtration through steel wool. Pattle and Burgess (1957) reported exposures of mice to kerosene smoke (354 mg./m.^{3}; dosage 106,200 mg. min./m.^{3}), without fatalities.

It was desired to obtain an estimate of the toxicity of black smoke which could be compared with similar estimates for other pollutants. It was evident that this would require a very high concentration of smoke, such as can conveniently be produced by burning tetralin (tetrahydronaphthalene, $C_{10}H_{12}$). The present work recounts experiments with this smoke; long-term observations on the survivors of these and other experiments are still in progress.

Methods

Production of Tetralin Smoke.—The smoke was produced by burning tetralin in an ordinary hurricane lamp (wick 13 mm. wide) with the glass and upper part removed. It gives a very smoky flame, and has the right flash-point for burning in this type of lamp; the combustion products are not irritant and have a faint smell of naphthalene. The consumption of tetralin was measured by weighing the lamp before and after the experiment; the fraction of the carbon content of the tetralin which was converted to smoke varied from 5% to 11%. The causes of this variation are not clear; it is important as it affects the concentration of smoke which can be obtained without overheating the chamber.

Exposure of Animals to the Smoke.—The animals were contained in cages within a chamber of 110 l. capacity in which the lamp also stood, and 20 or 25 l./min. of air

was blown into the top of the chamber through a tube 6 mm. in diameter; it thus entered with a velocity high enough (1·2 or 1·5 m./sec.) to give adequate stirring, and in quantity sufficient to prevent environmental anoxia. The chamber was opened every 30 min., when the animals were inspected and the relative positions of the cages were changed. The time at which each animal was found dead was noted.

The temperature in the chamber was kept at 29°C. or less by adjusting the wick of the lamp, so that the animals should not suffer from heat stroke. In experiment 4 the incoming air was cooled in ice so that a larger flame could be used without overheating.

In most of the experiments the animals were each kept in a separate small cage or compartment of a larger one, as it was thought that if they were allowed to associate they would protect one another. In some cases, however, a whole batch was placed in one cage. In some experiments the exposure was continued until all the animals in a batch had died; in others, batches were withdrawn while there were still survivors, so that the likelihood of delayed deaths could be assessed and the long-term effects of the exposure could be observed. The details of each experiment are recorded in Table 1.

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To measure this, a batch is exposed to a more or less uniform concentration of a toxic agent, and the time at which each animal dies is noted. From the known concentration the dosage to death, (Ct)D, of each animal is calculated, and the individual (Ct)Ds are treated statistically to obtain a value for the (Ct)D 50 and other data. For the greatest accuracy, the experiment should be continued until all the animals have been killed. If the toxic agent is one which rarely causes delayed deaths, the (Ct)D 50 will be nearly equal to the L(Ct) 50; this is the case with black smoke acting on mice. For agents such as phosgene, which commonly produce delayed death, measurements of the (Ct)D 50 would be of less value.

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A number of other exposures of animals to smoke from burning kerosene, from burning coal distillates, and from a diesel engine, have also been carried out. In some of these up to 20 p.p.m. of sulphur dioxide accompanied the smoke. The results have been in accord with those of the experiments recorded in Table 1.

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Microscopically the absence of oedema was con-

TABLE 1

ACUTE TOXICITY OF TETRALIN SMOKE

Experiment No.	1	1	2	2	2	3	4
Animals	Guinea-pigs	Mice	Guinea-pigs	Mice	Mice	Guinea-pigs	Rats
Conditions	Separate	Separate	Together	Together	Separate	Separate	Separate
Mean weight (g.)	264	17·8	190	20·2 (c)	21·2 (c)	190	190
Mean concentration of smoke (mg./m.³)	714	735	1,070	1,140	1,030	500	616
Duration of experiment (min.)	330	243	330	405	270	200	420
Mortality in chamber	10/10	18/25	10/10	25/25	9/25 (a)	0/10 (d)	1/10 (a)
(Ct)D 50 (mg. min./m.³)	159,000	147,000	204,000	351,000	311,000	—	—
95% confidence limits of	134,000	120,000	167,000	342,000	257,000	—	—
Limits of (Ct)D 50 (mg./m.³)	189,000	174,000	248,000	358,000	377,000	—	—
Slope (corrected for grouping)	8·5	5·4	8·0	21·3	8·1	—	—
Least (Ct)D (mg. min./m.³)	84,250	58,750	127,100	274,600	186,200	—	238,000
Greatest (Ct)D	229,600	178,920 (b)	352,600	462,100	274,600 (b)	100,000 (b)	260,000 (b)
Bliss factor *E*	1.00	1·15	1·00	1·00	2·58	—	—
Air supplied (l./min.)	20	20	25	25	25	25	25

(a) One further animal died 5 minutes after removal from chamber.
(b) Dosage at which survivors were removed.
(c) The two batches had been separated by randomization three days beforehand.
(d) Three animals died within 22 hours of removal from the chamber.

firmed and the smaller bronchi appeared to be blocked by soot. The liver, adrenals, and kidneys were normal.

In rats the picture was similar, save that the trachea was clearer. The failure of the lungs to collapse when the chest was opened was very marked.

A different picture was found in guinea-pigs, both in those which had died during exposure and in those which died later. The lungs did not collapse on removal from the body. There were numerous haemorrhagic, atelectatic patches; these were about 3 mm. across in the animals which died earliest, and gave place to larger haemorrhagic areas in those which survived the longest. The intervening areas were white and emphysematous, but a cut surface showed gross blackening of the lung. The patchwork of consolidated and emphysematous areas often resembled that produced in guinea-pigs by inhalation of sulphuric acid mist (Pattle, Burgess, and Cullumbine, 1956). The soot was found in the nasal passages but not in the trachea. The stomach contents were black; in some cases the stomach showed petechial haemorrhages. Microscopically the lungs showed oedema, emphysema, and some haemorrhagic consolidation.

The atelectatic areas could be re-inflated, and bubbles squeezed from the re-inflated portion resembled in their surface properties bubbles obtained from normal lung, it being thus inferred that the characteristic lining substance of the alveoli (Pattle, 1958) was still present in the atelectatic regions. Carboxyhaemoglobin was sought for in the dead animals by Lovibond's method, in which the colour of suitably diluted blood is compared with the colour of a standard series of glass discs; no trace of it was found.

Filtration of the Smoke by Fur.—As mentioned below, animals allowed to associate resisted the smoke better than animals in individual cages. The possibility of animals shielding one another from the smoke when huddled together was investigated as follows.

Two rats were anaesthetized with urethane. They were placed together on a flat surface so that the nose and mouth of one were buried in the pectoral fur of the other; the two were held in position by a loop of string. They were exposed to 1,190 mg./m.³ of smoke for 90 minutes. The nasal passages, trachea, and lungs of the animal which had breathed the smoke direct were blackened. On its pectoral fur, through which the other rat had breathed, was a ring of smoke deposit denser than elsewhere on the body. No smoke was found anywhere in the respiratory system of the rat which had breathed through the fur.

A similar experiment was performed with two mice with similar results.

In another experiment the chamber atmosphere was sucked through a belt of guinea-pig fur, 2 mm. wide, at right angles to the hairs; the smoke was completely filtered out by the fur.

Physical and Chemical Properties of Tetralin Smoke.—The smoke was entirely stopped by a Whatman No. 1 filter paper; this suggests that it consisted of aggregates of diameter not less than 0·5 μ. This was confirmed by examination of a sedimentation cell sample; most of the deposit consisted of fluffy aggregates and networks, the smallest particles visible being thin wisps a few microns long. Eighty per cent of the smoke passed through the cascade impactor (May, 1945), most of the remainder being deposited elsewhere than on the slides.

To measure the bulk density of the deposit, smoke was sucked through a Whatman No. 1 filter paper at an air velocity of 1·1 cm./sec., and the weight and thickness of the deposit were noted. The bulk density was found to be between 0·03 and 0·04; the bulk density of soot scraped from the walls of the chamber was about 0·015. The deposit contained about 4·6% of tarry matter.

Changes in the *p*H of liquids when smoke deposit was added to them were investigated to see whether the smoke had any acid content which might account for its action on guinea-pigs, a species which may be fatally affected by sulphuric acid mist in concentrations as low as 12 mg./m.^{3}; and also because city smokes appear to have a buffering action which interferes with estimations of acids in fog.

When 1 g. of smoke deposit was added to 50 ml. of 25% ethyl alcohol (a liquid which wets the deposit) at *p*H7, the *p*H was hardly altered. The *p*H of a similar mixture containing 1 mg. of sulphuric acid to 50 ml. of liquid was 3·4; this rose to 3·6 when 1g./50 ml. of smoke was added. It is thus clear that the effects of the smoke cannot have been due to its acid content, and that the buffering action of this particular smoke in the acid range is slight. At *p*H9 the smoke showed feebly acidic properties; 1 g. neutralized about 10^{-4} mole of alkali.

Discussion

Toxicity of Black Smoke.—The figures displayed in Table 1 show that the (Ct)D 50s for mice and guinea-pigs are of the same order of magnitude; the values for the heavier mice are rather larger than those for the smaller mice. The value estimated for rats is of the same order.

In the experiments with mice in which there were survivors, 27 died in the chamber, one died five minutes after removal, and 22 survived. This suggests that the L(Ct) 50 for mice is only a little (perhaps 1%) less than the (Ct)D 50. The same probably holds for rats, in which similar lesions occur.

In guinea-pigs the lesions are different, and delayed deaths much commoner. Assuming a value of 8 for the slope of the graph of probit of total mortality against log. dosage, one may estimate the L(Ct) 50 for guinea-pigs as about 116,000 mg./m.^{3}, or 75% of the (Ct)D 50; this accords with the fact that in experiment 3 the L(Ct) 30 was probably slightly less than the (Ct)D 10. Apart from the animals which died during or within 24 hours of the experiment, there were no deaths within one month of exposure.

The results suggest that animals allowed to associate together protect one another against the smoke; this is probably due to their huddling together and their fur acting as a filter. No explanation can be given of the very high slope found in experiment 2, when 11 out of 25 associating mice died within half an hour.

In the mice and rats the lethal effects of the smoke appear to be due to blockage of the air passages by carbon particles, or by a secretion induced by them; it seems likely that low-density aggregates can be retained in the lung by an interception mechanism, in spite of their low impactability (May, 1945) as compared with droplets of similar size. The apparently smaller toxicity to the more mature mice used in experiment 2 and to the rats may be due to less easy blockage of the air passages in these animals.

In the guinea-pigs the haemorrhagic lesions and the late deaths leave no doubt that the effect of the smoke is of a different kind. They suggest that the smoke acts as a direct irritant to the air passages causing bronchial spasm, with attendant increased negative intrathoracic pressure. This leads to capillary haemorrhage and compensatory emphysema, so that irreversible damage is done to the lung without serious external signs.

The lesions in guinea-pigs resemble those produced by sulphuric acid mist, but the experiments on the chemical properties of the smoke show that its actual acid content is negligible.

Application to Atmospheric Pollution.—Both black smoke and sulphur dioxide have been blamed for the lethal quality of fog, and are the only pollutants whose concentrations in the London fog of 1952 are known; it is therefore of interest to compare the acute toxicity of tetralin smoke, as measured in these experiments, with that of sulphur dioxide in similar concentrations. This has been done in Table 2.

The L(Ct) 50s for tetralin smoke acting on mice and guinea-pigs have been estimated above. Weedon, Hartzell, and Setterstrom (1939) found that when guinea-pigs and mice were exposed to sulphur dioxide in concentrations varying from 170 to 3,000 mg./m.^{3}, 33% of the total deaths caused took place after the animals had been removed from the gas. Late deaths were about as common among mice as among guinea-pigs. We may, therefore, suppose that a dosage which kills 33% of the animals during the exposure will afterwards kill a further 17%, *i.e.*, we may equate the (Ct)D 33 with the L(Ct) 50. Values of the (Ct)D 33 have been obtained from the data of Weedon *et al.* (1939), and from the records of Pattle and Burgess (1957), and are given in Table 2 as the L(Ct) 50.

It will be seen that judged by the L(Ct) 50s, tetralin

TABLE 2

DOSAGE AND EFFECTS OF SOME ATMOSPHERIC POLLUTANTS

Pollutant	Animal	(mg./m.³)	L(Ct) 50 (mg. min./m.³)	Source
Tetralin smoke	Mouse	735 to 1,140	146,000 to 348,000	Current work
Tetralin smoke	Guinea-pig	500 to 1,070	116,000 to 153,000	Current work
Combustion products of coal	Rat	57	>4,200,000	Vintinner and Baetjer (1951)
Sulphur dioxide	Mouse	800	2,160,000	Weedon *et al.* (1939)
Sulphur dioxide	Mouse	2,560	1,030,000	Pattle and Burgess (1957)
Sulphur dioxide	Mouse	2,430	579,000	Weedon *et al.* (1939)
Sulphur dioxide	Guinea-pig	797	3,460,000	Weedon *et al.* (1939)
Sulphur dioxide	Guinea-pig	2,800	1,535,000	Pattle and Burgess (1957)
	Data for London fog of December 5 to 9 (at County Hall)			
City smoke	Man	4·46 (max.) (b)	23,400 (a) (b)	Scott (1953)
Sulphur dioxide	Man	3·8 (max.)	19,600 (a)	Scott (1953)

(a) Mortality of order 0·1%; dosages quoted are maxima.
(b) Estimated by stain method.

smoke is some 10 times more toxic to mice, and some 25 times more toxic to guinea-pigs, than is sulphur dioxide in similar concentrations.

Scott (1953) records the concentrations of smoke and sulphur dioxide at County Hall, London, in the London fog of 1952. The smoke concentrations were measured by stain blackness, a method which is subject to errors due to variation in the composition of the smoke. On the assumption that these data are accurate, the total dosages available to a person who stayed in the open at County Hall during the whole five days (December 5 to 9, 1952) of the fog have been calculated and are given in Table 2. It will be seen that the dosage of smoke available was greater than that of sulphur dioxide. In the smog there was thus more London smoke than sulphur dioxide, while tetralin smoke is more toxic to animals than is sulphur dioxide. It would, however, be unsafe to regard this as an indication that smoke was the main toxic agent in the 1952 smog, for city smoke differs in composition from tetralin smoke, and the concentrations in the toxicity experiments were much higher than those in the smog. The particles in a smoke as dense as that used in the experiments are also bound to form aggregates, even if their initial size is similar to that of particles in city smoke; many of the particles in the latter resemble carbon black (Cartwright *et al.*, 1956). Moreover, sulphur dioxide sometimes has a bronchoconstrictive effect on human beings in concentrations as low as 1 p.p.m. (2·7 mg./m.³), while there is no evidence that tetralin smoke in this concentration has any effect. It is not therefore possible to draw any conclusions from the animal experiments in relation to the London smog, save that black smoke from burning tetralin, in dosages similar to those of London smoke available in the 1952 smog, has no detectable acute effect on animals.

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SOME HAZARDS IN THE MANUFACTURE AND USE OF PLASTICS

BY

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From Imperial Chemical Industries Ltd. (Plastics Division)

(RECEIVED FOR PUBLICATION JANUARY 13, 1959)

The expansion of the plastics industry during the last few years has introduced the possibility of hazards from new polymers and from modifications to old products. The first two sections of this paper deal with the diminishing incidence of dermatitis in synthetic resin plants using formaldehyde and with the toxic properties of some chemicals added during the manufacture of polyvinyl chloride compositions. After a brief reference to the hazards of catalysts used in the manufacture of new polymers in the polythene series, an account is given of the dangers of polytetrafluoroethylene. At high temperatures this important new polymer gives rise to decomposition products that may be harmful when inhaled, and smoking contaminated tobacco is one of the commonest ways in practice by which workmen may be affected. Animal experiments have confirmed the dangers of excessive heating of this polymer although the symptoms differ from those in human beings so that it is still not possible to incriminate any one of the products evolved at these temperatures. In a description of the hazards of manufacture of copolymers of butadiene that are new to this country the toxic properties of the monomers are given in some detail since some of these could prove harmful to the factory worker unless adequate precautions are taken, although the final materials are inert and free from danger.

There is an increasing demand for the use of plastics by the general public and in specialized fields. They are widely used in the food industry and for domestic articles so that it is important that both the raw materials and the final article will not contaminate food or beverages. None of the constituents of the plastics should be capable of being extracted by the food or drink with which they come into contact, but in order to ensure this it is more convenient in practice to submit them in the first place to the action of a few selected solvents. Depending on the results of these initial experiments the materials may subsequently have to be submitted to pharmacological tests which may take several weeks to be completed. Three unusual problems in this field are described.

The most difficult application in which to ensure freedom from danger is probably in the surgical use of plastics. Surgeons already have wide experience of the technique of handling and using plastics. Although the effects of a few selected plastics have been investigated and described, the response of living tissues to these materials is often unpredictable. The results of implantation in many patients will not be available for several years and it is suggested that the misuse of plastics in this field presents dangers that may not always be appreciated.

The growth of the plastics industry over the last few years has been such that there are few people nowadays who are unfamiliar with at least some of its products. Their application for domestic purposes alone has made them well known to the public, but this represents only a small section of the field in which plastics are proving useful and often essential materials. It is this continually increasing diversity of uses, together with the ability of the chemist to synthesize new polymers or macromolecules, that chiefly suggests the extraordinary

OUTPUT OF PLASTICS

Country	Thousands of Tons							
	1950	1951	1952	1953	1954	1955	1956	1957
Great Britain	155	195	180	210	274	316	338	393
France	33	40	35	53	85	100	127	160
Germany	98	168	190	241	326	400	480	580
Italy	23	26	29	52	77	122	141	125
Japan	18	42	50	65	87	128	200	278
U.S.A.	825	895	882	1,045	1,134	1,442	1,544	1,800

possibilities of future expansion in the industry. The striking post-war development may perhaps be most clearly demonstrated by the foregoing table showing the quantities of plastic raw materials produced in various countries.

In view of this rapid growth it should hardly be necessary to emphasize the need for ensuring the health and safety, not only of those engaged in the manufacture of the products, but of the millions of people who use them. Protection of the workmen in the factory is ensured without much difficulty by adopting principles of occupational hygiene, but the use, for example, of the final plastic material for food containers or in surgery needs careful consideration and frequently a detailed investigation of the product and its ingredients. A typical example is in the stringent regulations applied to packing materials by the Food and Drugs Administration of the United States (Lehman, 1956).

The basis of every plastic material is the polymer and this is synthesized today from chemicals made from such basic products as air, water, salt, lime, coal, petroleum, fluorspar, and agricultural products. The pathological effects which may result from the more common plastics and their constituents have been described by Mallette and Haam (1952a and b), Wilson and McCormick (1955), Parmeggiani and Sassi (1955), Hine, Kodama, Anderson, Simonson, and Wellington (1958), and Oettel (1957).

It is proposed in this paper to deal mainly with hazards associated with plastics manufactured by a chemical organization which is the largest single manufacturer of plastics raw materials produced in the British Commonwealth. The paper includes comparatively recent developments in plastics and their applications, and it can be regarded as a supplement to a previous publication (Harris, 1953) which originally described one or two of the compounds to which further reference will now be made.

Individual Plastics

Formaldehyde Products.—Formaldehyde is used in very large quantities in the plastics industry, principally in the manufacture of urea formaldehyde and phenol formaldehyde resins and moulding powders. It is known to be an acute poison and skin irritant (Schwartz, Tulipan, and Peck, 1947). Its effects on the skin and by absorption have already been described (Harris, 1953) so that only a brief reference to the subject is necessary here. In synthetic resin plants using formaldehyde the incidence of dermatitis has gradually been reduced to negligible proportions in recent years although production has increased by roughly 50%; the number of men employed has diminished over the last five years.

A new and larger plant began production in 1952 and the men had to accustom themselves to a strange environment, with frequent modifications of the process at first, while maintaining a reasonable standard of production (Table 1). As the new plant was situated in a different part of the country from the old, several of the men who accepted a transfer from one to the other had to readjust themselves to new domestic as well as industrial environments while others were newly engaged with no previous experience of the chemical industry. These facts may account to some extent for the high incidence of dermatitis during the early days at the new plant, whereas, during the last three years there have been few cases of dermatitis (Evans, 1958).

TABLE 1
DERMATITIS IN FORMALDEHYDE PLANTS

	Year	Average No. of Workers (approx.)	No. of New Cases of Dermatitis	Change of Employment on Account of Dermatitis	Lost Time Cases
Old Plant	1945	150–250	9	High labour turnover	1
	1946		10		6
	1947		11		1
	1948		9		4
	1949		16		2
	1950		15		2
New Plant	1952	275	29	Nil	1
	1953	270	45	14	1
	1954	260	15	3	3
	1955	230	4	Nil	—
	1956	225	7	Nil	—
	1957	220	2	Nil	—

Only five men lost time in the new plant and 17 were transferred to other employment on account of dermatitis, most of them in one year. Ninety-five per cent of the men who developed dermatitis in the new plant were successfully treated while continuing at work and lost no time. This compares with 77% who similarly lost no time in the old plant, an improvement which was probably associated with a number of factors. The new plant has improved and more conveniently situated washing facilities. There has probably also been a tendency over the years for men who are prone to develop dermatitis to seek other employment of their own accord.

Polyvinyl Chloride.—This material is made by polymerizing the narcotic gas vinyl chloride (CH_2:CHCl). The pure polymer is inert and neither toxic effects nor dermatitis have been experienced by those who have handled it for several years. Plasticizers, stabilizers, lubricants, pigments, and other substances are frequently added to it, in order to modify its physical properties, and, since any of these may slowly leach or be extracted from the final article, it is essential to ensure that they are harmless, especially for certain uses.

A typical example is the commonly used plasticizer tricresyl phosphate, the ortho-isomer of which is a notoriously dangerous poison. Its effects have been fully described (Hunter, 1955) and the most recently reported outbreak occurred in 1955 in Durban and involved 11 people (Susser and Stein, 1957). An interesting feature of the latter occurrence is the fact that it probably arose from drinking water stored in contaminated drums that had been taken from a local paint factory where "this compound was freely used without special precautions".

Derivatives of phthalic acid, which are often used as plasticizers for polyvinyl chloride, are almost all of a low order of toxicity. This has been shown by Mallette and Haam (1952b) and Smith (1953), and the negligible chronic toxicity of the widely used di-2-ethylhexyl phthalate has been demonstrated in animal feeding experiments by Harris, Hodge, Maynard, and Blanchet (1956). A worker who mistakenly swallowed a tablespoonful of the rather more toxic dibutyl phthalate developed bilateral keratitis with albumin and blood cells in the urine within 48 hours (Cagianut, 1954). He recovered after 14 days in hospital and the case is of interest since the compound has been freely used on the human skin as an insect repellant (*British Medical Journal*, 1947).

Lead salts may be added to polyvinyl chloride as heat or light stabilizers and may constitute a hazard if they are used in powder form. A report by Goss and Ross (1953) suggested that the use of lead paste eliminated the danger of poisoning by inhalation, but in fact this only applies provided good general, and especially local, exhaust ventilation is installed and regularly inspected. In addition such an apparently fool-proof method of suppressing dust does not eliminate the necessity for routine estimations of lead in the atmosphere to ensure that the level is kept below 0·15 mg./cu. metre.

Cadmium compounds are sometimes used as stabilizers or pigments for polyvinyl chloride and a comprehensive literature exists on their toxicity (Fairhall, 1957a). Most of the reported cases of poisoning have been due to ingestion of the soluble salts of cadmium. Gabby (1950) has shown, however, that insoluble pigments such as calcined cadmium sulphide and selenide were harmless when relatively high concentrations were ingested by experimental animals. This is comparable with the extreme toxicity of soluble barium salts as opposed to insoluble barium sulphate, large quantities of which are daily consumed by patients as barium meals for radiological investigations (Smith and Cook, 1948).

To ensure that the plastic material in which these pigments are incorporated is free from toxicity it must also be shown for certain specialized applications that they cannot be extracted by such solvents as those mentioned below under "Food Applications". Workmen must not be exposed to the risk of inhaling dust or fume emanating from soluble or insoluble compounds.

Reference books almost without exception describe tin and its compounds as relatively harmless substances and Fairhall (1957b) states that it is one of the least toxic of the common metals when ingested as a salt. These statements are true with regard to tin itself and many of its inorganic salts which are insoluble in water, but certain organic tin compounds such as the alkyl derivatives are soluble and readily absorbed. In recent years the latter derivatives have been used more and more as heat stabilizers for polyvinyl chloride, especially in its unplasticized form. Stoner, Barnes, and Duff (1955) demonstrated that many alkyl tins are toxic to animals and stressed the need for care in handling these compounds during manufacture, as some of them can be absorbed through the skin. Barnes and Stoner (1958) confirmed these findings in a more detailed investigation of a larger number of alkyl tin compounds, but they drew attention to the fact that some of the higher homologues, such as the dioctyl and dinonyl derivatives, are relatively harmless, whether absorbed by mouth or applied to the skin in large doses. Both these papers refer to the disastrous occurrence in France when several deaths were reported as the result of the oral administration of diethyl tin diiodide to patients. Apart from the higher homologues already mentioned, therefore, all alkyl tin derivatives should be excluded from plastic materials likely to be used in contact with food, unless it is shown that they cannot be extracted from the plastic.

Polyolefines.—In addition to polythene, other plastics are now being manufactured from polymerized unsaturated hydrocarbons of the olefine series and some of these processes involve the use of catalysts that may be dangerous. Aluminium alkyl compounds of a low molecular weight, for example, are used for this purpose and they are spontaneously inflammable in air so that difficulty may be experienced in handling them. Knap, Leech, Reid, and Tamplin (1957) described the hazards of these compounds and drew attention to the possibility of pulmonary damage in experimental animals exposed to their fumes. For safety aluminium alkyl compounds are usually handled in solution but even so they can produce burns that are extremely painful and usually slow to heal.

A research worker suffered burns as a result of splashes from a small quantity of a 20% solution of an aluminium

alkyl compound which blew out of a chemical flask. Although the patient's skin and eyes were immediately irrigated, he suffered painful burns of the neck, shoulder, both hands, and the left eye. Irrigation of the eye was prolonged and uninterrupted while he was conveyed to hospital by ambulance after the burns had been covered with dry sterile dressings. Two days later the skin had blistered but thereafter healing proceeded satisfactorily with treatment by exposure and the administration of systemic penicillin and early physiotherapy. The eye burn healed within a few days. The incident stresses the importance of immediate and prolonged irrigation in such cases.

Polytetrafluoroethylene.—Polymers made from fluorine compounds possess exceptional properties which make them most useful plastic materials, one of the most important of which is polytetrafluoroethylene ("fluon"). The monomer is of a low order of toxicity but its purification results in the production of highly toxic residues; the process is therefore totally enclosed and handling is by remote control for the protection of the worker. The final polymer is extremely inert and is unaffected by strong acids, alkalis, or solvents and is harmless to experimental animals when ingested.

A sample containing about 21% polytetrafluoroethylene was incorporated to the extent of 0·5% by weight in the diet of a group of rats of both sexes. The experiment lasted about seven months after which no ill-effects were observed and no difference was noted in the average body weights of the experimental and control groups of animals. Histological examination of the body organs revealed no abnormality.

The influenza-like attacks that result from inhaling the fume emanating from this polymer when it is heated to high temperatures have already been reported (Harris, 1951). Sherwood (1955) described the clinical details in seven workmen affected in this way and observed that all but one of the men smoked at work. One or two particles of the polymer burnt on a cigarette seem sufficient to cause the fever. Sherwood states that smoking contaminated tobacco is probably the most likely cause of this condition, certainly more probably than machining or turning the product on a lathe, which was formerly considered to be a possible source of the fume.

A typical case was that of the workman engaged on machining the polymer who complained to his foreman of headache and shivering attacks and thought he was suffering from influenza. The foreman for reasons best known to himself thought the man was possibly malingering but allowed him to stop work and go home. Since it was an urgent job the foreman decided to finish it and incidentally helped himself to tobacco and cigarette papers that had been left on the machine by the workman. Later that evening in his home he developed a headache, tightness of the chest, and attacks of shivering, and he too thought that this was due to influenza. He went to bed and passed an uneventful night and the next morning both men returned to work having fully recovered. The symptoms, the obvious latent interval in the case of the foreman, and the rapid recovery are typical of the fever produced by polytetrafluoroethylene fumes.

Experimental work shows that fumes begin to be evolved when the polymer is heated above 250°C.; at higher temperatures exposed animals died of pulmonary oedema.

Rats were exposed to the fumes emanating from samples of "fluon" heated to 250°C., 275°C., and 300°C. for periods of six hours. At 250°C. there were no ill-effects. At 275°C. the rats showed signs of irritation but recovered after exposure. Post-mortem examination showed no abnormality. At 300°C. the vapours were lethal. Respiratory distress occurred after four hours' exposure and at necropsy the lungs were discoloured and oedematous but other organs appeared normal. A histopathological examination of the lungs showed severe congestion with some areas of haemorrhage and oedema but again no abnormality was found in other organs.

The offending decomposition product is unknown but Zapp, Limperos, and Brinker (1955) gave the results of a detailed investigation of the products evolved at different temperature ranges. Above 500°C. the decomposition of the polymer proceeds rapidly enough to make it possible to identify the products in that particular range which consist of tetrafluoroethylene monomer, other fluorocarbon gases, a high boiling residue, and traces of hydrogen fluoride. The most toxic compound was found to be octafluoroisobutylene, which is lethal in a few hours to rats in concentrations as low as 0·5 p.p.m., but it cannot be regarded as the causative agent since the symptoms produced in animals are different from those in man.

Butadiene Copolymers. The combination of two monomers in the manufacture of a plastic material is not new and a typical example of such a copolymer is that made by polymerizing a mixture of vinyl acetate and vinyl chloride. One of the most important synthetic chemicals used today in the manufacture of plastics is butadiene which is produced at the rate of nearly a million tons annually. Although capable of polymerization on its own, it is mainly combined for this purpose in industry today in varying proportions with monomers such as styrene, acrylonitrile, or methyl methacrylate to give a wide range of products. Depending on the relative proportions of the monomers the final materials vary in

composition from hard resins to soft rubbers, some of which have become widely known as synthetic rubbers. Suspensions of these copolymers are also used in emulsion paints, for coating printing paper, and as bases for leather finishes and non-woven fabrics. Each monomer will now be considered separately.

Butadiene (*Vinyl Ethylene* $CH_2{:}CHCH{:}CH_2$).—This is a gas with a very low order of toxicity, acting as a mild narcotic only in such high concentrations (Carpenter, Shaffer, Weil, and Smyth, 1944) that the safe level for factory atmospheres has been set at 2,500 p.p.m. Wilson, Hough, and McCormick (1948) state that there is no apparent systemic injury to human beings in concentrations below 5,000 p.p.m. In one investigation by Wilson (1944) a group of workmen exposed to butadiene vapour and complaining of symptoms were immediately examined (including chest radiographs and blood examinations) with negative results, as also were the follow-up examinations.

Styrene (*Vinyl Benzene* $C_6H_5CH{:}CH_2$).—This is an oily liquid which is a moderate skin and mucous membrane irritant possessing anaesthetic properties in high concentrations (Clinton, 1948). It has a characteristic disagreeable odour, and Spencer, Irish, Adams, and Rowe (1942) suggest that the extreme nose and eye irritation produced in man by a concentration of 1,300 p.p.m. affords a definite safeguard against voluntary exposure to acutely hazardous concentrations. Men exposed to styrene fumes and complaining of toxic effects were sent to hospital for examination (including complete blood count and chest radiograph) and no pathological condition was found even in men who were observed for at least one year subsequently (Wilson, 1944). The maximum permissible concentration in the atmosphere in any factory should not exceed 100 p.p.m.

No case of poisoning or dermatitis due to styrene has occurred in the plants considered here but one incident is quoted to stress the importance of anticipating every contingency and of avoiding paying undue attention to the effects of only the main chemicals being handled.

Three men working in the packing section beneath a drier became ill with nausea and vomiting and were taken to the medical department where they quickly recovered after treatment. It was assumed that they had been exposed to excessive amounts of styrene vapour, apparently the only substance present which might have caused the illness. The plant was temporarily closed to improve the ventilation and two days later two other men engaged on this task were overcome with nausea, giddiness, and headache. They were escorted to the ambulance room where they recovered after rest and oxygen therapy. No clinical abnormality was found and they were sent home.

An immediate inspection of the packing cubicle after the second incident revealed a smell of coal gas which was in fact oxidized in order to supply the drier with atmospheric nitrogen so as to eliminate an explosive hazard in the process. Analyses showed 0·15% carbon monoxide in the atmosphere at working level, which had accumulated as the result of a leak from a faulty valve. This is a dangerous concentration of carbon monoxide which can lead to unconsciousness and possibly death in about two hours (Johnstone, 1941).

Schwartz (1945) is of the opinion that most of the occupational dermatitis occurring in the manufacture of certain butadiene—styrene copolymers is caused by chemicals added to make the reaction possible and is not due to either monomer.

Acrylonitrile (*Vinyl Cyanide* $CH_2{:}CHCN$).—This is a colourless liquid which acts as a systemic poison resembling cyanide when absorbed by ingestion, inhalation, or through the intact skin. There is little or no evidence that it has a cumulative effect (Dudley, Sweeney, and Miller, 1942). A summary of its properties, uses, and methods of safe handling is given by the Manufacturing Chemists Association (1949). Brieger, Rieders, and Hodes (1952) demonstrated high cyanide levels and the presence of cyanmethaemoglobin in animals exposed to the vapour, proving that the toxicity of acrylonitrile is based on the formation of cyanide in the body. This had been suggested by Dudley and Neal (1942) who found that the injection of sodium nitrite had a protective and antidotal action on animals. Although a few cases with symptoms—such as nose, throat, eye, and skin irritation, headache, jaundice, and a low-grade anaemia—have been reported (Wilson *et al.*, 1948), no fatality or even serious poisoning has occurred in industry where thousands of tons of acrylonitrile have been manufactured and handled. Dudley and Neal (1942) described one case in a laboratory worker who spilled small quantities of the liquid on his hands and later developed blisters, peeling, and cracking of the skin.

Rubber gloves are not a satisfactory protection as the liquid dissolves rubber, but they may be used for short spells when handling the latices or partially polymerized materials. Contamination of the skin demands immediate and prolonged irrigation, and treatment of systemic poisoning is identical with that of cyanide poisoning (Potter, 1950). Eye irrigation bottles and cyanide first aid equipment must be readily and conveniently available in selected places on the plant, and a special cyanide emergency kit such as that described by Lloyd (1957) should be kept in the medical department on sites where acrylonitrile is made or handled. Atmospheric concentrations should not exceed 20 p.p.m. No incidents have

occurred in the plants under review but considerable precautions are taken in the form of enclosed processes, good ventilation, and education of the worker.

Methyl Methacrylate (CH_2:$C(CH_3)COOCH_3$).—This monomer has already been described as an extremely mild irritant and toxic by inhalation (Deichmann, 1941) but only in such high concentrations as over 1,000 p.p.m.

The hazards of all monomers mentioned in this section are confined to the manufacturing process and may only be experienced in the factory as the result of accidents or unsatisfactory environmental conditions. Apart from rare cases of sensitization the polymers are inert and harmless.

The Uses of Plastics in Containers for Food

There is a rapidly growing demand for plastic articles for use in contact with food and beverages, which is not surprising in view of their lightness, inertness, clean appearance, and durability. The list of such applications is already extensive but below are a few typical examples together with some of the polymers from which they are made:—

Application	Polymer
Tubes for conveying liquids	Polythene, polyvinyl chloride
Wrapping films	Polythene, polystyrene, polyethylene terephthalate
Coated paper cartons	Polythene, formaldehyde products
Beakers, cups, bowls, bins	Polymethyl methacrylate, polystyrene, polythene, urea formaldehyde
Bakers' roller mills (linings)	Polytetrafluoroethylene
Food conveyor belts	Nylon, polyvinyl chloride
Gears, bushes, and mixing machinery	Nylon
Refrigerator trays and linings	Polyvinyl chloride, polystyrene
Soft drink containers and dispensers	Polymethyl methacrylate, polystyrene

The manufacturers of plastic articles should ensure that food or drink is not affected by them, as this might constitute an offence against Sections 1 and 2 of the Food and Drugs Act, 1955. It is fortunate that the inert property that renders plastic materials useful in this and other fields also generally implies that the product is harmless. It has already been mentioned, however, that plastic materials may contain other chemicals besides the polymer and in certain circumstances these additives may be extracted by the food or beverage in contact with the plastic product. Lead salts, for example, are readily extracted from plasticized polyvinyl chloride so that they rapidly contaminate liquids conveyed in tubes made from this product.

Attention has already been drawn to the fact that the solubility of a substance influences its degree of toxicity, *e.g.*, lead, cadmium, barium, and tin compounds, so that the initial and sometimes only investigation required to ensure that plastic materials are harmless is to determine whether the products or their ingredients are soluble in, or can be extracted by, the food with which they will be in contact. Lehman (1951) states with regard to food packaging materials that if the film or any of its components may be shown to be insoluble, there is no problem of toxicity. He emphasizes, however (Lehman, 1956), that the tests demand extremely sensitive analytical methods if they are to be of any value.

The obvious substance to use for extraction tests is the food itself but the practical difficulties of microanalysis make it simpler in practice to use a range of solvents of known strength. For this purpose the following minimum list, to which others may be added if experience makes it necessary, has recently been suggested by the British Plastics Federation (1958):—(*a*) Distilled water, (*b*) a 5% w/v aqueous solution sodium carbonate (anhydrous), (*c*) a 6% w/v aqueous solution hydrochloric acid, (*d*) a 50% w/v aqueous solution of ethyl alcohol, and (*e*) olive oil (B.P.C.) to which 2% w/w of oleic acid has been added. Extraction should be carried out at about 60°C. for as long as a week or even a month. The conditions of extraction are described in detail by the British Plastics Federation (1958); they do not differ to any great extent from those recommended by Lehman (1956). In all cases of doubt or lack of knowledge, the degree of toxicity of the chemical substances present must be assessed by pharmacological methods which may involve prolonged investigations. The information that such toxicity tests should provide and some of the considerations which govern the conditions of use of toxic materials in general have been described by the Medical Research Council (1957). One or two practical problems may be of interest.

(*a*) Polythene tubing has proved valuable for conveying cold water under difficult conditions of terrain over long distances, such as those experienced in providing water for agricultural needs. The inert tubing normally does not in any way affect the water. Polythene is known, however, to be pervious to gases and one or two instances have occurred where the water has been contaminated by leaking gas or sewer mains lying near the plastic tube.

(*b*) Polytetrafluoroethylene has proved a useful material for lining bread and cake tins and coating dough rollers as it prevents the food adhering to the equipment. Extraction tests on this product gave negligible results and, as shown above, prolonged feeding tests had no effect on the health of experimental animals. Coppock and Knight (1957) found that traces of fluorine were absorbed from these linings when they were first heated. The amount absorbed, however, could be reduced to consider-

ably less than the proposed limit for the fluorine content of self-raising flour (Ministry of Agriculture, Fisheries and Food, 1957) if the lined containers were subjected to suitable initial heating before use.

(*c*) Bottles manufactured from one particular nylon copolymer were said to impart an unpleasant flavour to liquids contained in them. This was found to be due to the extraction from the product of small quantities (0·2% on prolonged boiling) of low molecular weight constituents. Acute and chronic toxicity tests of this extract showed that (1) no ill-effects were observed in a group of rats receiving six oral doses of 0·5 to 2 g./kg. of the extract in arachis oil solution for eight days compared with control animals which received the oil only. No abnormality was found post mortem. (2) The extract was given to a group of young rats in their drinking water in a concentration of 400 p.p.m. This dose was continued for nearly six months during which time no ill-effects were observed and the average weights at the end of the period compared favourably with those of the control animals. Post-mortem and histological examination of the body organs showed no abnormality.

These findings, however, do not justify the use of the nylon copolymer for this application since the liquid was contaminated albeit by a harmless substance.

The Use of Plastics in Surgery

Probably the most decisive evidence of the safety of the use of selected plastics in contact with food and consumable liquids is provided by the large number of successful implantations in human tissues for surgical purposes.

An increasing number of surgical uses is being found for plastics but only a brief reference to the subject can be made here. The results in general are very encouraging but it must be admitted that unsuitable materials are sometimes selected by surgeons because they fail to seek technical advice about the properties of the products. The result can bring into disrepute plastic materials which might otherwise be of inestimable benefit to many patients.

A variety of surgical applications of plastics was described by Ingraham, Alexander, and Matson (1947) and by Bing (1950), and a brief summary was given in a leading article in the *British Medical Journal* (1952) but there is some divergence of opinion in these and other accounts about the reaction of the tissues to plastic implantations. Most reports and the now extensive experience with these materials confirm the inert nature of many of them, especially when they contain no additives or these cannot be extracted by tissue fluids. There is a tissue response, however, as shown by LeVeen and Barberio (1949), who investigated the effects of implanting four different plastics in dogs and found that "teflon" (polytetrafluoroethylene) was the only polymer that did not produce a proliferative foreign body reaction. Scales (1953b) described tissue reactions to a few synthetic materials but it appears that such reactions are usually due to misuse of the plastic, such as subjecting it to highly mobile or weight-bearing conditions (Newman and Scales, 1951). Nylon cups fitted on the femoral head become abraded when they are subjected to weight-bearing so that fine particles of the polymer cause a proliferative tissue reaction with areas of necrosis; six instances of this unsuitable use of the material have been described by Scales (1957).

Most of the unsatisfactory applications have occurred in orthopaedic surgery, where plastics have been very extensively used. One of the most popular but least satisfactory applications has been the acrylic hip prosthesis (Judet and Judet, 1950) of which a large number have proved failures (Pridie, 1953), and the biomechanical and other problems involved in this arthroplasty described by Scales and Zarek (1954) and by Buxton (1955) should be carefully studied if this operation is contemplated. A detailed account was given by Scales (1958b) of the problems involved in the use of plastics and metals in prosthetic surgery.

In contradistinction to these findings Seddon and Scales (1949) inserted a polythene substitute for the upper part of a diseased femur which to date has been successful (Scales, 1958a). A man suffering from polyostotic fibrous dysplasia with a long history of pathological fractures of the femur had the bone replaced by an acrylic prosthesis (Figs. 1 and 2) which still proved satisfactory after seven years (Burrows, 1958). Another patient had undergone many operations over a period of 26 years for osteomyelitis of the femur but still suffered pain that treatment, including lumbar sympathectomy, had failed to relieve, and Bingold (1954) replaced the diseased stump with an acrylic prosthesis which has resulted in "a completely painless stump with a full range of movements" (Bingold, 1958). Although these patients have artificial limbs it should be emphasized that in each case the prosthesis bears no weight.

The importance of selecting precisely the right material in its most suitable form is emphasized by Moloney (1958) who investigated the results of nylon repairs of herniae in over 2,000 cases. He found that monofilament suture material was the most satisfactory and produced better results than the braided type in these operations.

FIG. 1.

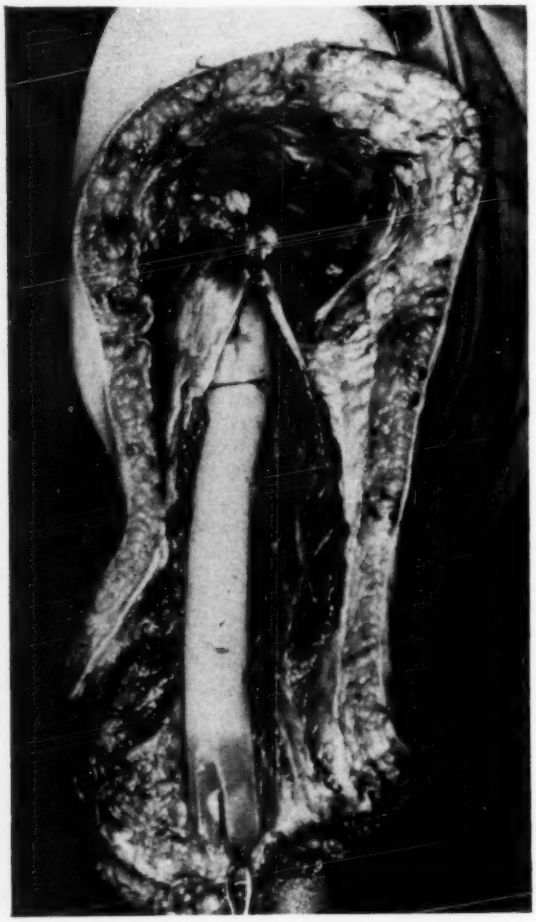

FIG. 2.

FIG. 1.—Acrylic prosthesis for the upper part of the femur.
FIG. 2.—Acrylic prosthesis inserted in the thigh.

By courtesy of the Institute of Orthopaedics.

Eastcott and Wilson (1958) record the use of "orlon" (polyacrylonitrile) cloth for an aortic graft which for over two years proved almost inert to the host cells and tissues and produced negligible reaction although functioning efficiently during this time.

Valvular prostheses have been used in cases of aortic insufficiency by Hufnagel, Harvey, Rabil, and McDermott (1954) who described the results as extremely encouraging. Hufnagel (1955) states that an acrylic valve fixed by nylon rings has been inserted in the aorta in about a hundred cases and concludes that the procedure has been of value for patients with this disability.

Another interesting application has been the intraocular implantation of an acrylic substitute for the lens of the eye in cases of cataract. Ridley (1956) asserts that no more effective treatment for monocular cataract has yet been devised. He has now performed about 600 acrylic lens operations and states that the material can be tolerated in the human eye for eight years and, as far as we can tell, indefinitely (Ridley, 1958).

These few examples indicate that plastic implantations in tissue may remain for many years without toxic or initiative effects. An extensive bibliography on the subject has been compiled by Grau (1956).

Conclusion

It is seldom that a group of materials has invaded the everyday lives of people as rapidly as plastics and

yet the industry is still in its infancy. With the exception of food and drugs few substances can have been subjected to such thorough investigations to ensure freedom from harm to those who make and use them. This continues to be essential and all manufacturers of the raw chemical materials should be provided with extensive laboratory facilities and a modern technical service to deal with the problems that arise in the fabrication and use of plastics.

In a well-balanced reference to the subject Dodds (1953) states that the moral is to perfect the system of investigation and control which would seem to be a more practicable solution than to suppress or ban the use of chemicals.

In the surgical field it is suggested that a more cautious approach is indicated by the failures due either to misapplication or sometimes to the use of the wrong plastic materials. It might seem unnecessary to suggest that each patient ought to be considered as an individual case but the production of thousands of Judet acrylic prostheses in a few different sizes without adequate laboratory investigation (Scales, 1953a) indicates that patients are often in fact not treated in this way. The wide use of plastics in orthopaedic surgery demands a very close liaison between the surgeon and the designer of the plastic prosthesis before, during, and after the operation. Ideally it also requires the provision of a special workshop as a separate department in any large orthopaedic hospital where the plastic appliance can be adequately prepared and tested. When suitably designed for selected cases plastic prostheses have proved invaluable.

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PATTERNS OF SICKNESS ABSENCE IN A RAILWAY POPULATION

BY

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This investigation was carried out in order to obtain morbidity statistics in a large industrial population with special reference to the effects of ageing.

The population chosen, the "railway research population," consisted of a sample of Scottish railwaymen, drawn from five of the eight areas in the Scottish Region of British Railways. Only certain occupational grades were studied.

Information was obtained over a period of one year by means of a detailed monthly return of (*a*) sickness absence data and (*b*) job changes. Indices of sickness absence were defined. The sickness absence experience of the railway research population was compared with that of other populations. It is a healthier group than the total insured population but differs in some respects from that of London Transport.

The nature of sickness absence within the railway research population was then studied. It was shown in all but one measure used that sickness tends to increase with age, the most important factor being the increase of long episodes. Examination of the frequency distribution of the duration of sickness episodes revealed that sickness absence tends to be taken in terms of weeks off rather than days off.

Analysis of the daily variation in sickness absence showed that the total absence rate increased from Monday to Friday. There was a well defined tendency for sickness to start on Mondays, and in longer episodes an additional tendency to start on Fridays. This was interpreted in terms of morale, both positive and negative.

Marked differences of the same order of magnitude as those due to age were noted in the sickness experience of the various grades, related to both conditions of work and responsibility.

The reasons for job changes were analysed and the grades to which men were transferred were identified. The choice of suitable grades for older workers was discussed.

It was concluded that working conditions might be important factors in the type of sickness absence experienced and that comparisons with other populations might be helpful in this context. More detailed work was also called for on the psychological as well as physical aspects of the work situation for both the individual and the grade.

The study of occupational health has, in general, been conducted by examination of the association between specific diseases and specific occupations through the medium of specific irritants. Studies of the aetiology of the dust diseases and of industrial bladder tumours are usually of this type. From the standpoint of the identification of pathological entities and the promulgation of preventive regulations, this method has had great success. This has led some to consider that the disease-centred approach is the only method available at present of assessing the health of the industrial worker. We dissent from the implications of this view and maintain that it is possible to make meaningful statements about health as a general concept, *i.e.*, not only in terms of the absence of disease, but also, for example, in terms of the amount of sickness absence from work that is experienced by the individual. Sickness absence is a direct social concomitant of ill-health and thus its amount makes a good first approximation to a measurement of health. This sort of measurement would be particularly useful, for example, in comparing the relative healthiness of certain groups in the population. Of course, further refinement and other measures will have to be incorporated before a satisfactory, measurable definition of health is arrived at, but it seems to us that this method of successive approxi-

mations, the validity of which can be measured, is a most useful one.

Partly because the emphasis has been on disease and partly because of difficulties in obtaining information, most past investigators have been concerned with the disease-centred approach, *i.e.*, consideration of the incidence of diseases in terms of episodes or spells. As we are interested in the health and adaptation to work of people, we have so organized our data as to get a continuous record for each person over the period studied and our analysis will be predominantly person-centred.

We wish to present these data as a contribution to the small amount of person-centred information at present available.

The Present Investigation

The present investigation was undertaken in order to collect morbidity statistics for a large industrial group. In addition, it was to serve as preliminary material upon which to frame hypotheses and to allow for the isolation of subgroups for further study.

Relevant data were obtained on a sample of railwaymen in Scotland, which will be referred to as the "railway research population." The sample was restricted to five of the eight areas which comprise the Scottish Region of British Railways (the areas left out being the rural north). The railway research population was further limited to the nine largest of the 20 departments of the Scottish Region. Within these nine departments certain occupations (grades) were chosen.

A difficulty that arose was that the existing system of grades on the railways did not appear suitable for research purposes. Many of the grades were extremely heterogeneous and contained within themselves large variations in actual tasks. It was therefore agreed that there should be included a selection of 27 grades, each clearly defined and chosen by the Scottish Regional Establishment and Staff Office so as to be typical of the different occupations on the railways. Since the focus of interest was more especially on the older age groups, none of the grades with predominantly young workers, *i.e.*, under 25 years of age, was included. The Regional Establishment and Staff Officer and his colleagues drew up a schedule in which the chosen grades are classified as to degrees of skill and responsibility, location and type of work, and other factors (Table 1).

In addition to the above, one further selection was made. The numbers in four of the 27 grades were too large to be dealt with and a sample of one in two was therefore taken from the grades of lengthman, locomotive fireman, signalman, and locomotive driver.

The railway research population thus consists of 14,074 men, which is 24% of all male employees on the railways in Scotland as given by the Registrar General's 1951 census.

After an initial census from which the age and length of service in present grade were obtained, a monthly return of all members of the railway research population was rendered to us for 12 months from April 1, 1955. This gave information on sickness absence and job changes.

Sickness Absence.—The sickness absence information consisted of: (1) Starting date of sickness episode (including day of the week); (2) finishing date of sickness episode (including day of the week); (3) the number of working days lost; (4) diagnosis; (5) hours worked in the week of the absence.

From this information the number, type and duration of sickness absences for each individual during the year were obtained and rates for various age and occupation groups were derived.

Two comments must be made on these data:

(1) The duration of an absence is given as the number of working days lost. Thus if a person is away for a week, this may mean the absence is counted as of five, six, or seven days' duration according to the number of days the absentee was scheduled to work during the particular week concerned. (Where an absence occurs when a half day is due to be worked, this is counted as a full day's absence.)

(2) In British Railways all people who are absent are required to provide a reason. If their absence is for three days or over, a medical certificate must be produced and in these cases the diagnosis is taken from the certificate. When the absence lasts for one or two days, the only admissible reason is still sickness, but the person's own description of the ailment is accepted. Thus all absence is "sickness absence" and we have for each occasion a "diagnosis" either as an item on a medical certificate or from the person concerned. It is appreciated that some of this short-term absence may be due to causes other than sickness.

Job Change.—The nature of and reasons for changes of jobs were also obtained.

Results

Percentage of Time Lost.—As a first overview of the health of the railway research population, we shall consider the percentage of time lost due to sickness.

The total number of days lost throughout the year was obtained. On the basis of a five and a half

TABLE 1

REPRESENTATIVE RAILWAY GRADES

Manual

With Little or No Responsibility

Sheltered from Weather

1. Goods porter
   Loading and unloading goods from wagons, etc.
2. Workshop labourer
   General labouring work within workshops

Exposed to Weather

3. Shedman
   General labouring work within motive power sheds
4. Lengthman
   Permanent way maintenance

Some Measure of Responsibility

Sheltered from Weather

5. Luggage room attendant
   Handling and stowage of passenger luggage deposited for temporary custody
6. Stores issuer
   Issue of stores within workshops and motive power depots

Exposed to Weather

7. Shunter (goods)
   Employed in goods shunting yard or sidings under supervision, attaching and detaching wagons, and assembling goods trains for despatch
8. Locomotive fireman
   Engine footplate train crew
9. Carriage and wagon examiner
   Examines rolling stock wheels, axles, axleboxes

Carrying Considerable Degree of Responsibility

Sheltered from Weather

10. Signalman
    Manipulating signal levers in signal box controlling section of the line
    Responsible for safe conduct of trains within his section
11. Locomotive fitter
    Artisan employed in workshops and motive power sheds
12. Pattern maker
    Artisan employed in workshops on the fashioning of patterns necessitating a high degree of accuracy

Exposed to Weather

13. Locomotive driver
    Engine footplate train crew. Thorough knowledge of signalling arrangements, rules, and regulations
14. Ganger
    Permanent way track maintenance. Has charge of length gang of between five and eight men. Equivalent to working foreman
15. Telegraph lineman
    Maintenance of electrical signal apparatus, telephone lines, and telecommunication installations
16. Head shunter
    Usually has one or more shunters under him and has to give directions

Sedentary

Routine Work—Little or No Initiative Required

17. Timekeeper
    Employed in workshops and motive power depots, etc. Maintains time records and does other routine clerical work
18. Shop officeman
    Employed in workshops
    Purely routine work
19. Clerk
    Routine clerical work in all departments

More or Less Routine but Requiring Some Measure of Initiative

20. Control staff
    Employed at static control points, supervising and regulating movements of rolling stock and traffic on running lines
21. Senior clerk
    Normally required to supervise small number of clerks

Requiring Considerable Measure of Initiative

22. Chief controller
    Responsible for the control and regulation of traffic, etc., on running lines in his area
23. Chief clerk
    Responsible for supervision and work of section of clerical staff

Administrative and Supervisory

Requiring Considerable Measure of Initiative and Mental Responsibility Exposed to Weather

24. Station master
    Supervision of station staff. Responsible for running of station from the operating and commercial aspects
25. Running shift foreman
    Supervision of staff in motive power sheds. Directly responsible to the shed master for provision and repair of locomotives
26. Yard inspector
    Supervision of shunting yard staff. Responsible for shunting operations including the assembling, despatch, and staging of goods trains
27. Permanent way inspector
    Supervision of permanent way maintenance. Has control of several gangs in a particular area

day week, the total man-days available for work were calculated and thus the percentage of time lost. The figures are:

Man-days lost in the year	..	116,742
Total man-days available	..	4,025,164
Proportion of time lost ..	..	2·90%

We compare this percentage with an equivalent figure derived from London Transport Executive (1956) on certain groups of their male employees. Their returns relate to a seven-day week and their figures are as follows:

Total man-days lost	.. ..	1,335,807
Total man-days available	..	50,243,345
Proportion of time lost ..	..	2·66%

The two estimates of the percentage of time lost are of the same order of magnitude. As these two proportions are only very general estimates, we shall not attempt any more direct comparisons (which would involve consideration of differences in the method of compiling the data and would entail an age standardization), but instead we shall compare age trends in the two populations. This is a more useful way of considering the data.

A further general comparison can be made with data derived from the sickness and injury benefit for the whole country given by the Ministry of Pensions and National Insurance (1956) report. This gives the days lost for sickness episodes of four days or more:

Total man-days lost..	..	201·77 million
Total man-days available	..	5,256·00 million
Proportion of time lost	..	3·8%

The comparative figures for the railway research population are as follows:

Total man-days lost (due to episodes of four days or more)	.. ..	113,173
Proportion of time lost	.. ..	2·8%

The proportion of time lost in the general population is higher than that in the railway research population. The extent of the effect of age is discussed later in regard to episode rate.

Indices of Sickness Absence.—We shall use the indices of sickness absence defined below. In all cases the population is that of the railway research population at the initial census. The corresponding nomenclature of the General Register Office's (1954) pamphlet is shown, but it must be appreciated that

to be directly comparable our own rates must be subjected to slight adjustment because of some differences in definition.

(1) *Sick Person Rate* (= 0·29).—The number of persons who are absent sick at some time during the year divided by the number in the population (General Register Office's period prevalence rate (persons)).

(2) *Episode Rate* (= 0·46).—The number of episodes or spells of sickness which are current at some time during the year, divided by the number in the population (General Register Office's period prevalence rate (spells)).

(3) *Average Duration per Person* (= 8·29 *Days Lost in the Year*).—The total duration within the year of all episodes of sickness that occurred wholly or partly within the year divided by the number in the population (General Register Office's average duration per person).

(4) *Average Duration per Sick Person* (=28·27 *Days Lost in the Year*).—The total duration within the year of all episodes of sickness that occurred wholly or partly within the year divided by the number of persons having at least one episode during the year (General Register Office's average duration per sick person).

(5) *Average Duration per Episode* (= 17·89 *Days*).—The total duration within the year of all episodes that occurred wholly or partly within the year divided by the number of such episodes (General Register Office's average duration per spell).

(6) *Average Number of Episodes per Sick Person* (= 1·58 *Episodes*).—The number of episodes of sickness which are current at some time during the year, divided by the number of people who are sick at some time during the year. (There is no General Register Office equivalent.)

We shall use each of these various indices at suitable times. For our own person-centred orientation, the two most useful indices to characterize a population are the sick person rate and the average duration per episode. For the purpose of obtaining comparisons with other work, we have also used the episode rate on a number of occasions.

Changes with Age in Railway Research Population.—Table 2 gives the values at various age ranges of the indices described above. (It should be noted that the 15-to-19-year-old group contains only 11 men and the rates for this age group are therefore not reliable.)

In general, it will be seen that all the indices, except the average number of episodes per sick person, have a definite age trend towards increasing sickness with age. It is, however, in those rates which incorporate duration that the age trend is the largest; for example, the average duration per person rises from four days lost during the year at age 20 to 24 to 15 days at 60 to 64.

Three general features of these age-specific rates may be noted.

(1) In the indices which do not incorporate duration, *i.e.*, the sick person rate and the episode rate, there is a mode at age 20 to 24. The rates then fall until age 35 to 39 and rise again in the later ages. We have as yet no explanation for this phenomenon.

(2) In the indices which incorporate duration, there is a marked increase with age. The fact that the change in the rates between ages 55 and 59 and 60 and 64 is much smaller than would be expected on this basis requires comment. Our hypothesis is that this lack of increase in the 60 to 64 age group is due to a separation of the more seriously sick people from the labour force. This is substantiated by a consideration of Table 3, derived from the job change data of the railway research population. This shows the percentage of railwaymen leaving the service due to health reasons or death. It will be seen that there is a big increase in the 55 to 59 age group. The majority of these separations were associated with some sickness absence during the year and would thus have been very likely to contribute to the amount of sickness absence at the 60 to 64 age group had they remained in employment.

For this reason it is maintained that at age 60 to 64 the employed railway population has a bias in favour of the healthier worker as compared with

TABLE 2

SICKNESS EXPERIENCE BY AGE IN A RAILWAY RESEARCH POPULATION

Index	Age Groups											
	15–	20–	25–	30–	35–	40–	45–	50–	55–	60–	65+	Total
Sick person rate	0·18	0·30	0·27	0·26	0·26	0·27	0·28	0·31	0·33	0·34	0·27	0·29
Episode rate	0·27	0·49	0·42	0·41	0·40	0·42	0·48	0·48	0·52	0·53	0·33	0·46
Average duration per person (days lost in the year)	0·45	4·29	4·29	4·85	5·10	5·89	8·12	9·52	13·78	15·04	9·75	8·29
Average duration per sick person (days lost in the year)	2·50	14·33	15·62	18·97	19·91	25·94	28·52	31·13	41·18	43·75	35·50	28·27
Average duration per episode (days)	1·67	8·71	10·33	11·84	12·71	16·28	17·04	19·66	26·31	28·59	29·24	17·89
Average number of episodes per sick person	1·50	1·65	1·51	1·60	1·57	1·59	1·67	1·58	1·57	1·53	1·21	1·58
N=	11	1,112	1,755	1,644	1,143	1,212	1,429	2,380	2,136	1,201	51	14,074

TABLE 3

PERCENTAGE OF RAILWAY RESEARCH POPULATION LEAVING SERVICE AT EACH AGE FOR HEALTH REASONS (INCLUDING DEATHS AND FATAL INJURIES)

Age Groups									
20–	25–	30–	35–	40–	45–	50–	55–	60–64	All
0	0·2	0·1	0·3	0·5	0·8	0·9	2·1	2·9	0·9

the notional total railway population (working, retired, or dead).

(3) There is a sharp drop in the rates for all measures except the average duration per episode in the 65 years and over age group. This would appear to be due to the fact that the normal age for retirement from railway service is 65 and it is only exceptionally that men are allowed to remain at work. It is obvious that those who do remain are a highly selected group in regard to health and adaptation to work.

Comparisons with Other Populations.—The comparisons with London Transport are shown in Figs. 1 and 2. London Transport regard all episodes of six months or over as being of six months only; and for all comparisons our own figures have been corrected on this basis. From these it is immediately obvious that the railway research population has a different pattern of sickness absence, having a much lower episode rate (0·46 as compared with 0·86), counterbalanced by a higher average duration per episode (16·94 days against 11·28), and this is true in all age groups. This is a striking and interesting difference and we should like to be able to pursue it further. To do this it would be necessary to compare a relevant occupation group in the first instance. A comparison of diagnostic categories would also be valuable. This has been done for one group, namely clerks (Pugh, Gordon, and Lévy, 1959).

Comparison with the total insured population is given in Fig. 3. In this case all episodes of three days and under are excluded, and our own data have been re-corrected in this respect. We again find that the episode rate for the railway research population is below that for the insured population at all ages (the figures for all ages combined are 0·30 as against 0·39). This would indicate that the railway staff are healthier than the population generally, unless the durations per episode outweigh this, which seems improbable. (Figures for average duration per episode are not available from the Ministry of Pensions and National Insurance.)

Fig. 1 shows that there is more variation with age in the episode rate for London Transport workers than with the railway research population. When the comparison is made with the total insured population (Fig. 3, only episodes of three days and over being considered) it is clear that there is a more

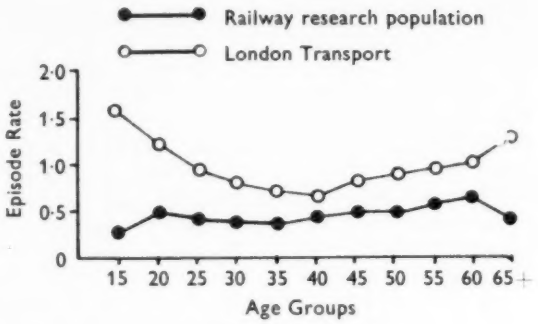


FIG. 1.—Episode rate.

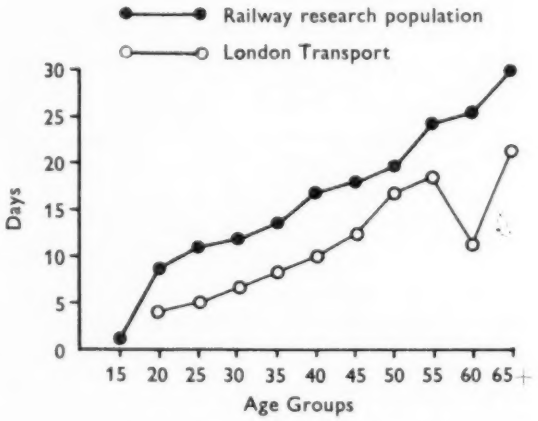


FIG. 2.—Average duration per episode.

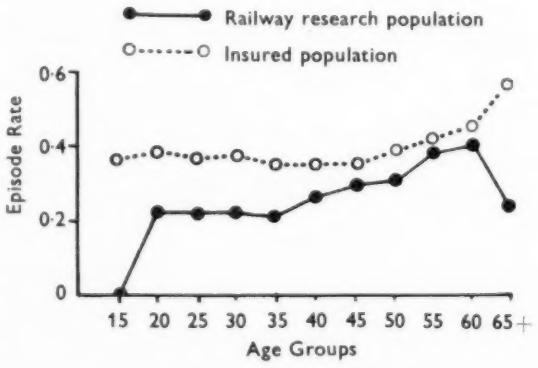


FIG. 3.—Comparison with insured population.

direct relationship between age and episode of sickness in the railway research population. The characteristic drop in the curves beyond the age of 60 is again to be noticed for the railway research population, but not for London Transport or the total insured population.

Duration of Episodes.—Fig. 2 shows that the average duration per episode becomes consistently longer with age in both London Transport and the railway research population. The length of episodes varied from one day to the whole year under consideration. An examination of the frequency distribution of the different episode durations was carried out. It was immediately apparent that the distribution was cyclic. The number of one-day episodes was large and the curve then fell steeply to four days. It then rose again for episodes of five and six days' duration. When the curve was followed through, it was seen that there was a peak at each multiple of five or six days. This cyclic pattern continued up to episode durations of the full year (Fig. 4).

It should be remembered that these episode durations are in working days lost and that the working week in British Railways is of five or five and a half days, five and a half days being counted as six for absence purposes (see above). Bradford Hill (1929) has demonstrated a somewhat similar cyclic pattern. He also found a tendency for sickness episodes to last for a week and, since he counted a week as of seven days' duration, this produced peaks at intervals of six, 13, 20 days, etc. He also found a lesser tendency for sickness episodes to end on the same day as they started, *i.e.*, to last eight days, and this produced lesser peaks at intervals of eight, 15, 22 days, etc. It is thus apparent that the cyclic nature of the distribution is caused by the fact that sickness absence periods (once one gets beyond the very short one- or two-day episodes) are more usually taken in terms of weeks off rather than days off.

There appeared also to be a secondary monthly cycle.

Type of Episode.—The recurrence of peaks at weekly and monthly intervals has provided a rationale for dividing the episodes into duration types; for example, up to a week, up to one month, up to two months, etc. To economize on types and because of the smallness of numbers, some amalgamations were made. But absences of up to two days' duration, since they do not require a medical certificate, have been considered separately. The final classification is thus as follows:

Type of Episode	Duration
Uncertified	1 or 2 days
Casual	3 to 6 days
Short	7 to 24 days
Medium	25 to 72 days
Long	73 days and over

Uncertified episodes refer to very short durations; casual episodes to those up to the week's peak; short to those up to the month's peak; medium to those up to the three month's peak; long episodes are those over three months.

Percentage Incidence of Types of Episodes.—The last two columns of Table 4 give the percentage incidence of types of episodes for the whole railway research population, together with the percentage of time lost due to each type of episode. In general, it will be seen that the percentages go in opposite directions. Whereas uncertified sickness provides the largest percentage of episodes, it provides the smallest amount of days lost and, while long sicknesses are smallest in number, they account for the highest proportion of days lost.

The breakdown of the percentage incidence of types of episodes by age groups is also given in Table 4. This demonstrates very strikingly the changing patterns of sickness absence with age. There is considerably less uncertified and casual absence among the older groups and considerably more medium or long episodes. Thus the increase in average duration per person with age (see Table 2) is not due to an increase in all types of episodes but to a selective increase in the longer durations.

Daily Variations in Sickness Absence.—There have been a number of studies of daily variations in sickness absence and many of these have concentrated on the "blue Monday" effect. This is the fact

TABLE 4

PERCENTAGE INCIDENCE OF TYPES OF EPISODE BY AGE

	Age Groups										Percentage of Total Episodes	Percentage of Time Lost
	20–	25–	30–	35–	40–	45–	50–	55–	60–	65+		
Uncertified	45·4	36·6	39·1	39·2	32·4	32·5	27·3	21·1	20·1	17·6	31·1	2·36
Casual	25·4	24·3	20·6	21·6	17·4	17·2	20·0	18·3	15·0	17·7	19·8	5·31
Short	22·4	30·5	30·0	27·0	34·3	30·2	32·0	33·3	33·9	29·4	30·8	22·40
Medium	5·5	7·3	7·7	8·9	11·5	15·5	14·9	17·8	19·8	17·7	12·9	31·50
Long	1·1	1·2	2·1	4·1	4·5	4·0	6·0	9·5	11·2	17·7	5·4	38·42
N = 100% =	548	729	673	459	513	681	1,153	1,119	632	17	6,527	116,743

TABLE 3

PERCENTAGE OF RAILWAY RESEARCH POPULATION LEAVING SERVICE AT EACH AGE FOR HEALTH REASONS (INCLUDING DEATHS AND FATAL INJURIES)

Age Groups									
20–	25–	30–	35–	40–	45–	50–	55–	60–64	All
0	0·2	0·1	0·3	0·5	0·8	0·9	2·1	2·9	0·9

the notional total railway population (working, retired, or dead).

(3) There is a sharp drop in the rates for all measures except the average duration per episode in the 65 years and over age group. This would appear to be due to the fact that the normal age for retirement from railway service is 65 and it is only exceptionally that men are allowed to remain at work. It is obvious that those who do remain are a highly selected group in regard to health and adaptation to work.

Comparisons with Other Populations.—The comparisons with London Transport are shown in Figs. 1 and 2. London Transport regard all episodes of six months or over as being of six months only; and for all comparisons our own figures have been corrected on this basis. From these it is immediately obvious that the railway research population has a different pattern of sickness absence, having a much lower episode rate (0·46 as compared with 0·86), counterbalanced by a higher average duration per episode (16·94 days against 11·28), and this is true in all age groups. This is a striking and interesting difference and we should like to be able to pursue it further. To do this it would be necessary to compare a relevant occupation group in the first instance. A comparison of diagnostic categories would also be valuable. This has been done for one group, namely clerks (Pugh, Gordon, and Lévy, 1959).

Comparison with the total insured population is given in Fig. 3. In this case all episodes of three days and under are excluded, and our own data have been re-corrected in this respect. We again find that the episode rate for the railway research population is below that for the insured population at all ages (the figures for all ages combined are 0·30 as against 0·39). This would indicate that the railway staff are healthier than the population generally, unless the durations per episode outweigh this, which seems improbable. (Figures for average duration per episode are not available from the Ministry of Pensions and National Insurance.)

Fig. 1 shows that there is more variation with age in the episode rate for London Transport workers than with the railway research population. When the comparison is made with the total insured population (Fig. 3, only episodes of three days and over being considered) it is clear that there is a more

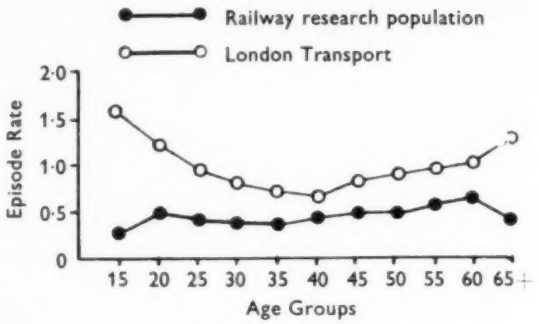


FIG. 1.—Episode rate.

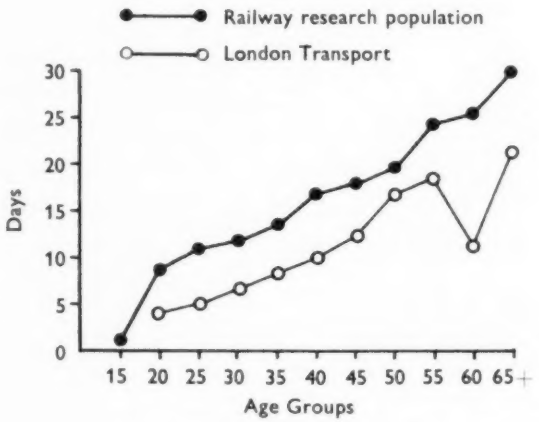


FIG. 2.—Average duration per episode.

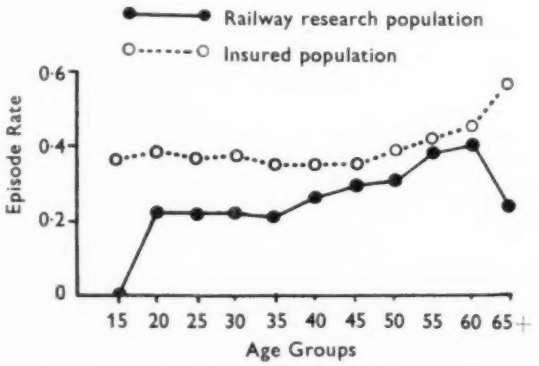


FIG. 3.—Comparison with insured population.

direct relationship between age and episode of sickness in the railway research population. The characteristic drop in the curves beyond the age of 60 is again to be noticed for the railway research population, but not for London Transport or the total insured population.

Duration of Episodes.—Fig. 2 shows that the average duration per episode becomes consistently longer with age in both London Transport and the railway research population. The length of episodes varied from one day to the whole year under consideration. An examination of the frequency distribution of the different episode durations was carried out. It was immediately apparent that the distribution was cyclic. The number of one-day episodes was large and the curve then fell steeply to four days. It then rose again for episodes of five and six days' duration. When the curve was followed through, it was seen that there was a peak at each multiple of five or six days. This cyclic pattern continued up to episode durations of the full year (Fig. 4).

It should be remembered that these episode durations are in working days lost and that the working week in British Railways is of five or five and a half days, five and a half days being counted as six for absence purposes (see above). Bradford Hill (1929) has demonstrated a somewhat similar cyclic pattern. He also found a tendency for sickness episodes to last for a week and, since he counted a week as of seven days' duration, this produced peaks at intervals of six, 13, 20 days, etc. He also found a lesser tendency for sickness episodes to end on the same day as they started, *i.e.*, to last eight days, and this produced lesser peaks at intervals of eight, 15, 22 days, etc. It is thus apparent that the cyclic nature of the distribution is caused by the fact that sickness absence periods (once one gets beyond the very short one- or two-day episodes) are more usually taken in terms of weeks off rather than days off.

There appeared also to be a secondary monthly cycle.

Type of Episode.—The recurrence of peaks at weekly and monthly intervals has provided a rationale for dividing the episodes into duration types; for example, up to a week, up to one month, up to two months, etc. To economize on types and because of the smallness of numbers, some amalgamations were made. But absences of up to two days' duration, since they do not require a medical certificate, have been considered separately. The final classification is thus as follows:

Type of Episode	Duration
Uncertified	1 or 2 days
Casual	3 to 6 days
Short	7 to 24 days
Medium	25 to 72 days
Long	73 days and over

Uncertified episodes refer to very short durations; casual episodes to those up to the week's peak; short to those up to the month's peak; medium to those up to the three month's peak; long episodes are those over three months.

Percentage Incidence of Types of Episodes.—The last two columns of Table 4 give the percentage incidence of types of episodes for the whole railway research population, together with the percentage of time lost due to each type of episode. In general, it will be seen that the percentages go in opposite directions. Whereas uncertified sickness provides the largest percentage of episodes, it provides the smallest amount of days lost and, while long sicknesses are smallest in number, they account for the highest proportion of days lost.

The breakdown of the percentage incidence of types of episodes by age groups is also given in Table 4. This demonstrates very strikingly the changing patterns of sickness absence with age. There is considerably less uncertified and casual absence among the older groups and considerably more medium or long episodes. Thus the increase in average duration per person with age (see Table 2) is not due to an increase in all types of episodes but to a selective increase in the longer durations.

Daily Variations in Sickness Absence.—There have been a number of studies of daily variations in sickness absence and many of these have concentrated on the "blue Monday" effect. This is the fact

TABLE 4

PERCENTAGE INCIDENCE OF TYPES OF EPISODE BY AGE

	Age Groups										Percentage of Total Episodes	Percentage of Time Lost
	20–	25–	30–	35–	40–	45–	50–	55–	60–	65+		
Uncertified	45·4	36·6	39·1	39·2	32·4	32·5	27·3	21·1	20·1	17·6	31·1	2·36
Casual	25·4	24·3	20·6	21·6	17·4	17·2	20·0	18·3	15·0	17·7	19·8	5·31
Short	22·4	30·5	30·0	27·0	34·3	30·2	32·0	33·3	33·9	29·4	30·8	22·40
Medium	5·5	7·3	7·7	8·9	11·5	15·5	14·9	17·8	19·8	17·7	12·9	31·50
Long	1·1	1·2	2·1	4·1	4·5	4·0	6·0	9·5	11·2	17·7	5·4	38·42
N = 100% =	548	729	673	459	513	681	1,153	1,119	632	17	6,527	116,743

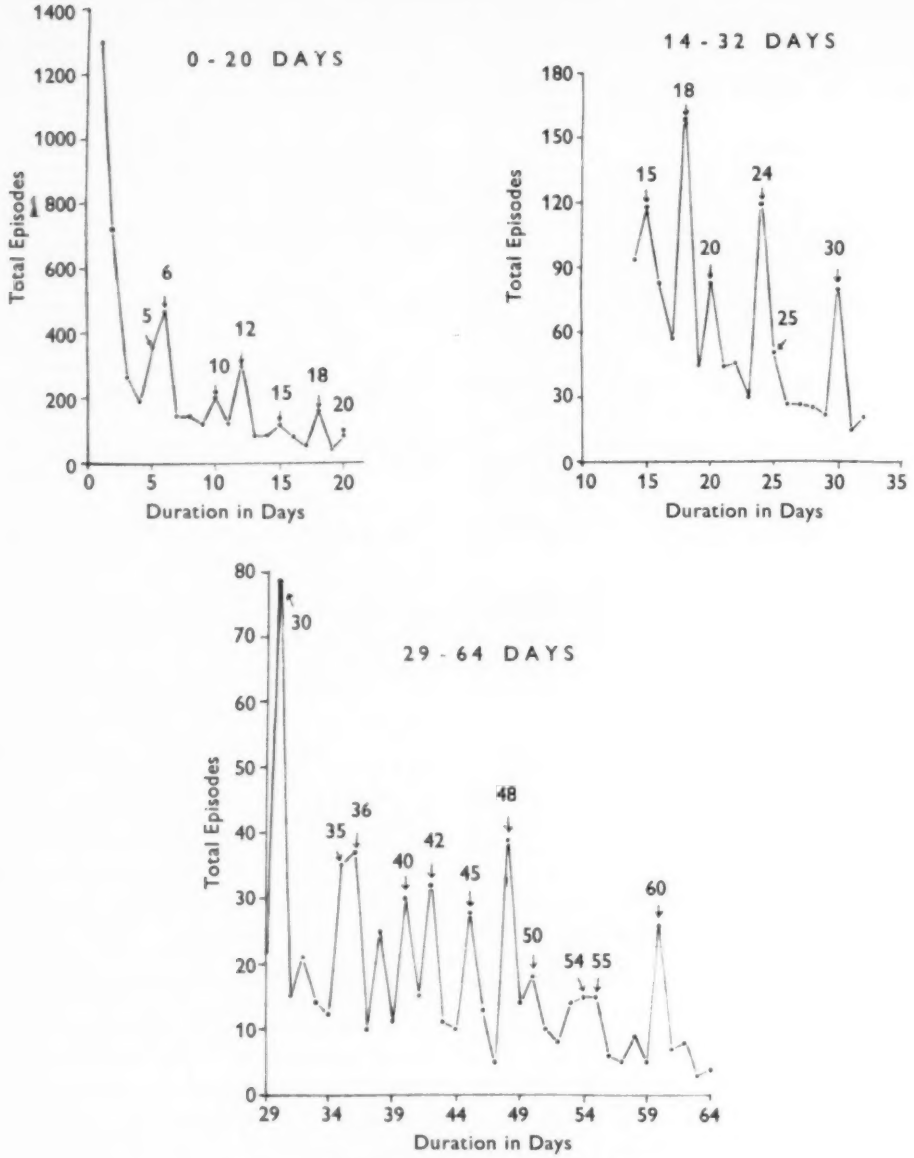


FIG. 4.—Frequency of episodes by duration (periodicity).

that the absence rate, *i.e.*, the percentage of man-days lost, is highest on a Monday and diminishes steadily during the week to its lowest point on a Friday. If one accepts the lower Friday rate as being a better estimate of "real" sickness, then it is usual to attribute the excess of Monday's absence over Friday's as being due to such factors as low morale.

Our own data on this question are summarized in Table 5. Only Monday to Friday is considered, since these days are worked by all grades.

It will be seen that for all sickness, the absence rate increases from Monday to Friday, and this is especially true of episodes of three days and over requiring medical certificates (certified sickness). This is generally considered to indicate high morale and a positive attitude to work. The rise in the rate may be explained by the effects of increasing fatigue

TABLE 5

DAILY VARIATIONS IN AMOUNT OF SICKNESS ABSENCE (PERCENTAGE OF MAN-DAYS LOST)

	Mon.	Tues.	Wed.	Thur.	Fri.
All sickness	2·73	2·77	2·80	2·81	2·84
Uncertified sickness	0·09	0·08	0·07	0·06	0·05
Certified sickness	2·64	2·69	2·73	2·75	2·79

and general strain as the week wears on, causing greater likelihood of succumbing to sickness.

We have also considered the daily variations in the five types of episode durations (see above). The general upward trend is reflected in all of them except the uncertified sickness. This shows a typical "blue Monday" effect in that the rate decreases from Monday to Friday (see Table 5). This contrasting slope suggests that uncertified absences, *i.e.*, those of one or two days' duration, are caused by different factors from longer episodes. Poor morale effects and reluctance to return to work after the weekend break may be relevant here. Behrend (1951) cites a similar result from a study of absentee rates among coal-miners in a normal working week in 1943. "The involuntary (unavoidable) rate shows a rising weekly absence curve, while the voluntary absence rate on the average shows a fall from Monday to Friday." There appears to be some inconsistency in characterizing populations in this way.

The Day of Starting Sickness.—There is another way of looking at these phenomena which bears some resemblance to that used by Bradford Hill (*op. cit.*). We have explored this topic by way of variations in the day of starting sickness. Table 6 shows that 45% of all episodes were started on a Monday. The breakdown of the various duration types is also given and it will be seen that more episodes of all types begin on a Monday than on any other day. (However, considerably more casual, short, medium, and long episodes start on this day than uncertified ones.) We have therefore combined all except the uncertified durations into one category, referred to as "certified episodes" (Fig. 5). As we have demonstrated, there is a tendency for these types of sickness absence to be taken in terms of weeks off rather than days off: it thus follows that since most sickness absence starts on a Monday, most must end on a Saturday, *i.e.*, most railwaymen return to work after an episode of sickness on a Monday. Bradford Hill noted a similar tendency in relation to day of starting and day of ending sickness absence.

The fact that half the certified episodes begin on a Monday strongly supports a high morale factor. It would appear that a disproportionate number of railwaymen manage to remain at work until the weekend before finally succumbing to sickness (or to consulting their doctor and being ordered to stay away from work).

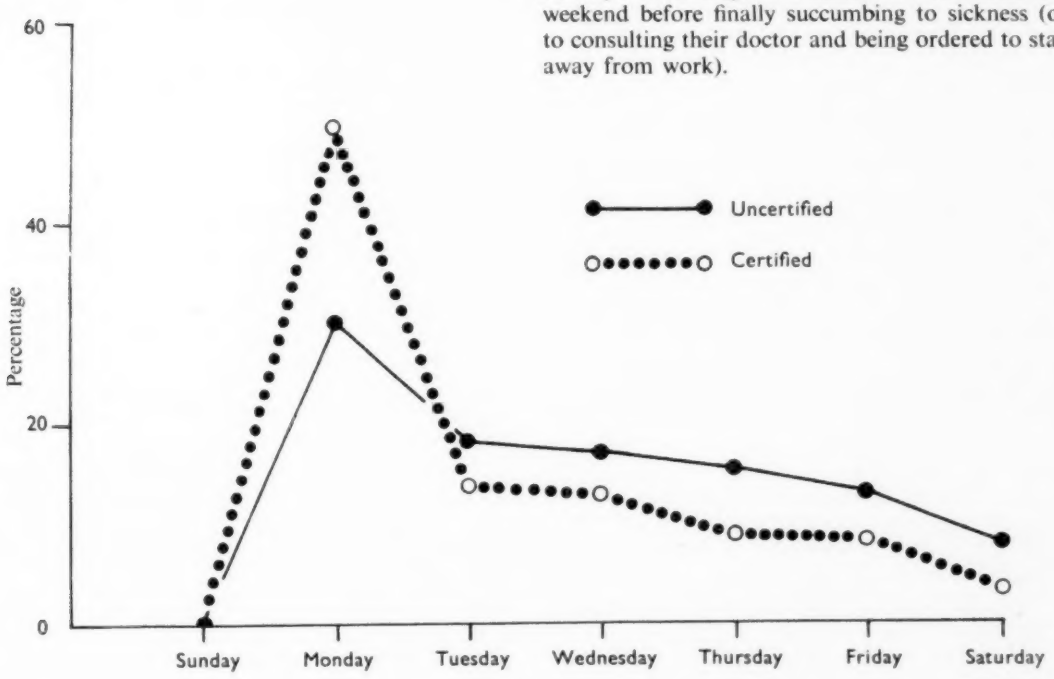
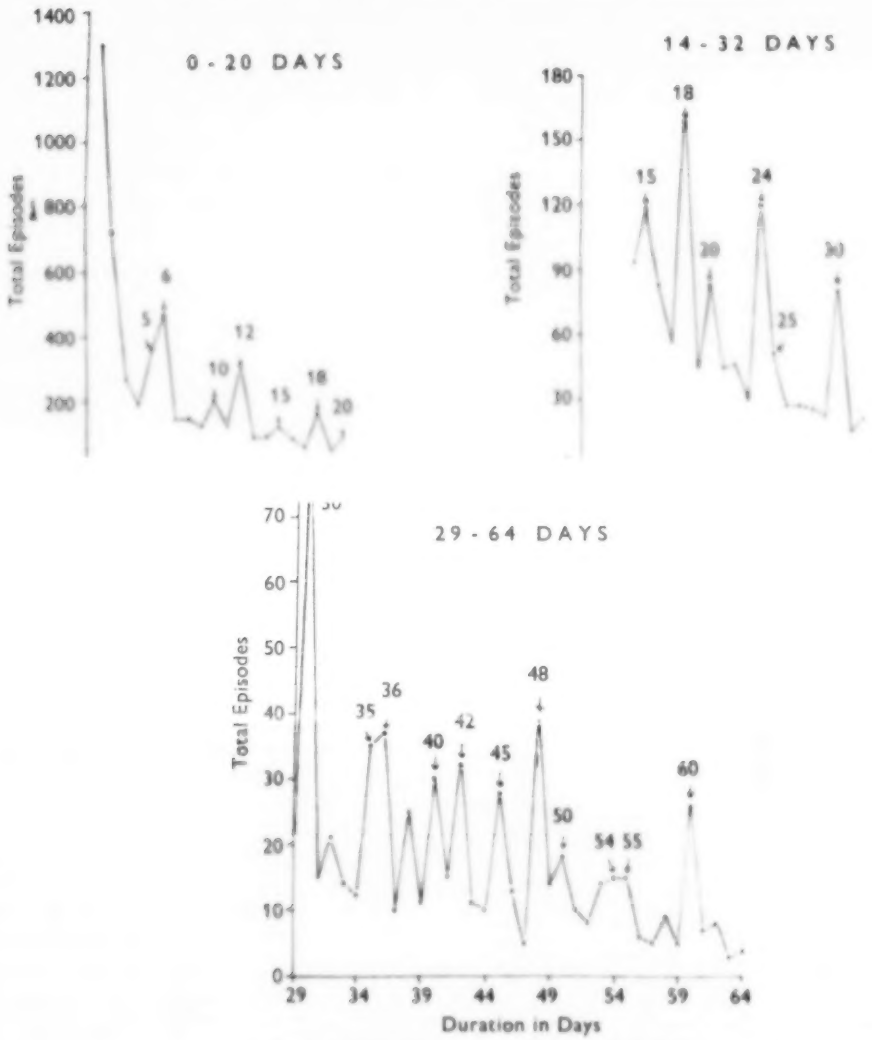


FIG. 5.—Comparison of starting day for certified and uncertified duration types.



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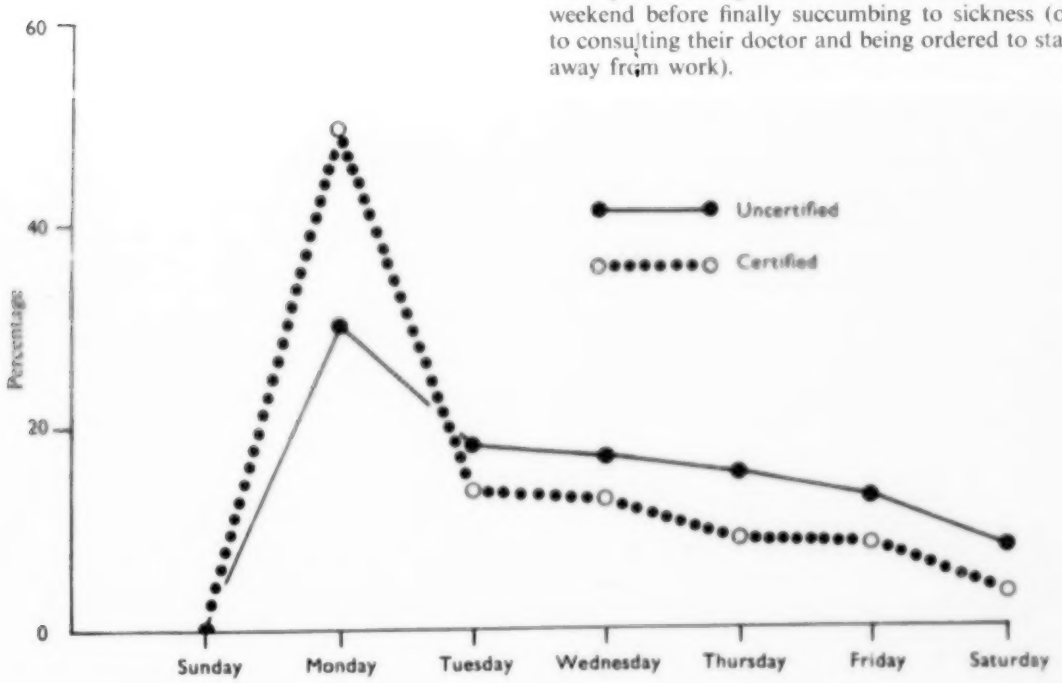

FIG. 5.—Comparison of starting day for certified and uncertified duration types.

Table 6 and Fig. 6 show an interesting trend with regard to the percentages of episodes starting on a Friday in the different types comprising certified episodes. It will be seen that a very small percentage of casual episodes start on a Friday; this, however, may well be related to pay day; a rather larger percentage of short episodes (comparable to the number of short episodes starting on Tuesday, Wednesday, and Thursday); and for medium and long episodes Friday is the most frequent day (after Monday) for starting a sickness. It would appear that as we move into the longer durations, it gets progressively more difficult for the man to remain at work until the weekend and increasing numbers succumb before this time. This is again evidence of high morale.

The effect of age on day of starting sickness has been examined, but no clear trends have been found beyond that expected because of the decreasing incidence of uncertified episodes in the older age groups.

The importance of considering the day of starting sickness together with the major support which it gives to the existence of a factor of high morale amongst railwaymen prompts us to revise the interpretation of the "blue Monday effect" based on daily absence rates in uncertified sickness. If there is a tendency to start sickness on Mondays (Table 6) and this is due to high morale, then the absences due to uncertified sickness will be *sui generis* higher on Mondays or Tuesdays than during the rest of the week. On this reasoning the decrease in absences from Monday to Friday may be due to high morale and not to low morale.

Clearly the examination of such problems must pay attention to variation in the days of starting sickness as well as daily variation in absence rates.

The Morale of Railwaymen.—In the preceding discussion we have suggested interpretations of the results in the morale terms commonly used by labour economists in this field. But further work is required in order to substantiate any hypotheses. Morale and effects of strain are psychological concepts and must be investigated in individual behaviour and attitude before they can be accepted as satisfactory explanations.

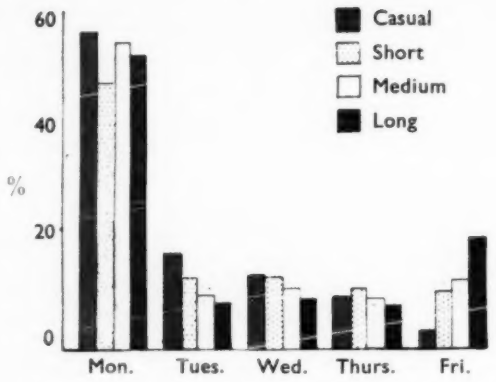

Fig. 6.—Day of starting sickness for certified duration types.

Sickness Absence Experience in the Various Occupations (Grades).—So far we have considered trends for the whole of the railway research population by age. We now come to consider differences in the various occupations or grades. As there are age trends in the population and varying age distributions in the grades, it is necessary to standardize for age. However, many age groups are often represented only slightly or not at all in some grades; for example, the lower age groups are not represented in the supervisory grades and the higher age groups are only slightly represented among the firemen. Thus the "indirect" method of standardization (Registrar General, England and Wales, Report, 1911) has had to be used. By the indirect method of standardization, the favourable or unfavourable nature of the age distribution of a particular grade, compared with the total population, is assessed in relation to sickness experience, and the recorded total sickness absence is increased or decreased as the case may be. The method is in fact one of handicap. The assessment of this handicap is as follows. The age specific sickness absence rate for the railway research population is

TABLE 6

DAY OF STARTING SICKNESS

Type of Episode	Percentage of Episodes Starting on a:							(N = 100%)
	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	
Total	1·90	45·00	14·48	13·56	11·08	10·13	4·86	6,527
Uncertified	0·30	29·85	17·64	16·85	14·78	12·32	8·28	2,030
Casual	0·31	56·53	16·91	13·20	8·80	3·09	1·16	1,295
Short	1·59	47·64	12·77	12·72	10·58	9·99	4·72	2,013
Medium	1·43	54·52	9·88	10·36	8·45	12·02	3·33	840
Long	1·43	52·15	8·02	8·31	7·16	19·77	3·15	349
Certified	1·18	49·61	13·05	12·07	9·41	9·14	3·31	4,497

TABLE 7

AGE STANDARDIZED RATES

Grade	Sick Person Rate			Average Duration per Episode (days)		
	Actual Rate	Age Standardized Rate	Rank	Actual Duration	Age Standardized Duration	Rank
1. Goods porter	0·46	0·43	3½	9·51	9·48	27
2. Workshop labourer	0·44	0·37	8	15·96	15·21	19
3. Shedman	0·27	0·27	15	33·12	29·34	2
4. Lengthman	0·27	0·27	15	22·53	22·36	5
5. Luggage room attendant	0·07	0·06	27	28·28	26·66	3
6. Stores issuer	0·40	0·37	7	19·41	17·17	17
7. Shunter (goods)	0·33	0·34	10	11·96	15·74	20
8. Locomotive fireman	0·22	0·24	20	12·49	21·29	7
9. Carriage and wagon examiner	0·23	0·23	21	19·73	20·75	8
10. Signalman	0·20	0·20	24½	21·53	20·57	9
11. Locomotive fitter	0·29	0·29	12½	15·52	17·35	16
12. Pattern maker	0·21	0·20	23	13·00	12·52	23
13. Locomotive driver	0·22	0·21	22	23·79	18·61	15
14. Ganger	0·20	0·19	26	24·20	19·32	12
15. Telegraph lineman	0·26	0·27	15	10·94	11·09	24
16. Head shunter	0·23	0·24	19	17·14	18·96	13½
17. Timekeeper	0·27	0·25	17	25·41	20·39	10
18. Shop officeman	0·42	0·41	5	24·44	21·47	6
19. Clerk	0·40	0·40	6	14·40	16·64	18
20. Control staff	0·42	0·44	2	6·81	10·02	26
21. Senior clerk	0·37	0·35	9	17·84	14·13	21
22. Chief controller	0·43	0·43	3½	14·62	13·95	22
23. Chief clerk	0·33	0·30	11	13·82	10·73	25
24. Stationmaster	0·26	0·25	17	25·62	22·54	4
25. Running shift foreman	0·32	0·29	12½	25·25	19·86	11
26. Yard inspector	0·53	0·48	1	24·81	18·96	13½
27. Permanent way inspector	0·22	0·20	24½	46·08	35·60	1
Total railway research population	0·29	0·29	—	17·89	17·89	—

applied to the particular grade and the numbers which would have occurred are summed over all age groups. This calculated figure for total sickness absence is then related to the actual. This figure is the standardizing factor which, when multiplied by the crude rate, gives the age standardized rate.

Considering the standardized rate of the two measures shown in Table 7, we see that there are wide grade variations on both of them, and indeed on the remaining indices not given in the table. The grade of yard inspector has the highest sick person rate (0·48) and the range goes from there to 0·06 for luggage room attendant, the rate for the whole railway research population being 0·29. The average duration per episode ranges from 35·6 days (permanent way inspector) to 9·4 days (goods porter) with 17·89 days for the whole population.

The figure given in Table 7 show clearly the large amount of variation due to differences in occupation. These seem to be quite as striking as the differences due to age.

The Relation between the Measures.—In characterizing a grade as being "sick" or "well" two measures seemed to be the most suitable; the sick person rate and the average duration per episode. These give respectively the proportion of men in the grade who have had a sickness and the average length of each episode. These measures between them incorporate the following variables for each grade: (*a*) Number of persons, (*b*) number of sick persons, (*c*) number of episodes, and (*d*) number of days lost. Thus they cover implicitly average duration per person, average duration per sick person, and the episode rate. In addition, they are logically independent, the first being based on (*a*) and (*b*) above and the second on (*c*) and (*d*). They have therefore been used as the two dimensions of sickness absence along which grades can be rated. Table 8 is a contingency table based on the quartiles for these two rates.

An interesting result was obtained when the two measures were correlated and the Spearman rank correlation (rho) was found to be −0·53. Thus there appears to be a very strong tendency for grades which are rated as sick on one measure to be rated as well on the other. This is demonstrated by a consideration of Table 8, where it will be seen that the first quadrant (the upper right hand quadrant representing those grades which are sick on both measures) and the third quadrant (those which are well on both measures) contain only three grades each, whereas the remaining second and fourth quadrants, *i.e.*, sick on one and well on the other, contain 11 and 10 grades respectively.

As the finding of a negative correlation between these rates is of some importance, we examined the effects of excluding (*a*) long durations, since relatively few of these episodes might have a marked effect, and (*b*) uncertified episodes, which may be qualitatively different from certified ones. The correlations

TABLE 8
SICK PERSON RATE AND DURATION PER EPISODE OF GRADES

Standardized Average Duration per Episode	Standardized Sick Person Rate			
	0·06–0·24	0·24–0·29	0·29–0·37	0·37–0·48
35·6–21·29	Permanent way inspector Luggage room attendant	Shedman Stationmaster Lengthman Locomotive fireman		Shop officeman
20·75–18·96	Carriage and wagon examiner Signalman Ganger	Timekeeper Head shunter	Running shift foreman	Yard inspector
18·61–15·74	Locomotive driver		Locomotive fitter Workshop labourer Shunter (goods)	Stores issuer Clerk
14·13–9·48	Pattern maker	Telegraph lineman	Senior clerk Chief clerk	Chief controller Control staff Goods porter

remained negative in both cases, being −0·36 and −0·16 respectively.

It may therefore be said that generally a grade has either a comparatively large number of people with short sickness episodes, *i.e.*, the "sick-well" grades in the fourth quadrant such as goods porter and chief clerk, or a smaller number of people with comparatively longer episodes, *i.e.*, the "well-sick" grades in the second quadrant such as permanent way inspector and shedman. In only a few instances can we consider a grade to be entirely sick or well; most grades are intermediate.

Relation of Sickness Absence Patterns to Certain Characteristics of Grades.—We now turn our attention to some features that may throw light on the causal relations underlying the negative correlations. We shall examine the sick person rate and that of average duration per episode in relation to the grade characteristics given in Table 1.

From Table 1 it is clear that the grades can be arranged along two dimensions concerned respectively with responsibility and conditions of work.

Responsibility.—This can be conveniently rated on a four-point scale with the following definitions:

Rating	Grades Characterized as:
1	(a) With little or no responsibility or (b) Routine work—little or no initiative required
2	(a) Some measure of responsibility or (b) More or less routine but requiring some measure of initiative
3	(a) Carrying considerable degree of responsibility or (b) Requiring considerable measure of initiative
4	Administrative or supervisory, requiring considerable measure of initiative and mental responsibility

Conditions of Work.—This dimension can be conveniently considered in three categories as follows:

Category	Grades Characterized as:
A	(a) Manual: exposed to weather or (b) Administrative and supervisory: exposed to weather
B	Manual: sheltered from weather
C	Sedentary

The grades and their ratings and categories are given in Table 9. It will be clear that these ratings are extremely crude categories and the dimensions themselves are defined only in the general terms given to us by British Railways' officials themselves. In this preliminary survey we made no attempt to refine the definitions or their categories, or to obtain empirical data on them. In such conditions only general indications can be revealed and correlation techniques are inappropriate as they are too elaborate for the data available.

There seems to be a clear relationship between conditions of work and the sick person and the duration per episode rates. The sick person rate is greatest in the least exposed conditions, while the duration per episode is highest where the exposure is greatest. In the ranking for the sick person rate (Table 9A) only one out of seven in the first quartile is exposed to the weather. On the other hand, in the first quartile of Table 9B (duration per episode) five out of seven are exposed to the weather, and in the fourth quartile (short duration per episode) only one out of seven.

The examination of the effect of responsibility shows that there is little or no change with the duration per episode, but that the sick person rate reveals some differences with responsibility. The rate is highest in the grades with least responsibility and vice versa. Thus in the first quartile (high rates) five out of seven have limited or no responsibility, while in the fourth quartile (low rates) five out of seven have substantial responsibility.

Our results in this sub-section, as far as they go,

TABLE 9

CERTAIN CHARACTERISTICS OF GRADES

Grade	Rank for Measure (Table 7)	Responsibility Rating	Conditions of Work Category	Grade	Rank for Measure (Table 7)	Responsibility Rating	Conditions of Work Category
A. Sick Person							
First Quartile				*Third Quartile*			
Yard inspector	1	4	A	Shedman	15	1	A
Control staff	2	2	C	Lengthman	15	1	A
Goods porter	3½	1	B	Telegraph lineman	15	3	A
Chief controller	3½	3	C	Timekeeper	17½	1	C
Shop officeman	5	1	C	Stationmaster	17½	4	A
Clerk	6	1	C	Head shunter	19	3	A
Stores issuer	7	2	B	Locomotive Fireman	20	2	A
Second Quartile				*Fourth Quartile*			
Workshop labourer	8	1	B	Carriage and wagon examiner	21	2	A
Senior clerk	9	2	C	Locomotive driver	22	3	A
Shunter (goods)	10	2	A	Pattern maker	23	3	B
Chief clerk	11	3	C	Signalman	24½	3	B
Locomotive fitter	12½	3	B	Permanent way inspector	24½	4	A
Running shift foreman	12½	4	A	Ganger	26	3	A
				Luggage room attendant	27	2	B
B. Average Duration per Episode							
First Quartile				*Third Quartile*			
Permanent way inspector	1	4	A	Locomotive driver	15	3	A
Shedman	2	1	A	Locomotive fitter	16	3	B
Luggage room attendant	3	2	B	Stores issuer	17	2	B
Stationmaster	4	4	A	Clerk	18	1	C
Lengthman	5	1	A	Workshop labourer	19	1	B
Shop officeman	6	1	C	Shunter (goods)	20	2	A
Locomotive fireman	7	2	A				
Second Quartile				*Fourth Quartile*			
Carriage and wagon examiner	8	2	A	Senior clerk	21	2	C
Signalman	9	3	B	Chief controller	22	3	C
Timekeeper	10	1	C	Pattern maker	23	3	B
Running shift foreman	11	4	A	Telegraph lineman	24	3	A
Ganger	12	3	A	Chief clerk	25	3	C
Head shunter	13½	3	A	Control staff	26	2	C
Yard inspector	13½	4	A	Goods porter	27	1	B

disclose the importance of both physical and psychological characteristics in sickness absence. The latter will be discussed further in relation to the three different levels of responsibility among the clerical grades in a further communication (Pugh *et al.*, 1959).

The Extreme Grades.—The three "sick-sick" grades, *i.e.*, those high on both measures, namely, shop officeman, yard inspector, and running shift foreman, and the "well-well" grades (those low on both measures) namely pattern maker, telegraph linesman, and locomotive driver, by those very facts merit further investigation. How far are these characteristics due to the nature of the work? How far do the "well-well" grades maintain their standards by shedding workers who fall sick? Are the "sick-sick" grades such as to tolerate more and longer absences without impairing efficiency and, if so, do they receive sick workers from other grades? These are some of the questions towards which further investigation will have to be directed.

Job Change due to Sickness.—Our information on job changes due to illness was subdivided according to whether the change was (*a*) instigated by the management, or (*b*) made at the request of the worker. Some of the receiving grades do not appear on our list of 27 grades, because they are jobs outside the scope of the railway research population although within the railway service.

There were 28 transfers by management and 13 at the request of the worker, due to sickness. Among these there were eight transfers within the same grade, leaving 26 grade-to-grade transfers by management and seven at "own request". These have been summarized in Table 10.

TABLE 10

JOB CHANGES DUE TO SICKNESS

By Management		*At Own Request*	
From:		From:	
Locomotive fireman	3	Locomotive fireman	2
Locomotive driver	7	Workshop labourer	1
Signalman	5	Shunter (goods)	1
Workshop labourer	4	Head shunter	1
Chief controller	1	Stationmaster	1
Others	6	Permanent way inspector	1
Total	26	Total	7
To:		To:	
Shedman	8	Shedman	2
Goods porter	3	Clerk	2
Workshop labourer	3	Goods porter	1
Clerk	3	Shunter	1
Stores issuer	2	Grades outside the survey	1
Yard inspector	1		
Grades outside the survey	6		
Total	26	Total	7

An interesting feature of the transfers not shown in the table is that the management transferred eight of the footplatemen (locomotive firemen and locomotive drivers) to shedmen, while both the locomotive firemen who transferred at their own request also went to shedmen. It is also worthy of note that the grade of workshop labourer is the only grade to lose and receive workers.

Grades which customarily accept workers transferred from other grades on grounds of health are referred to by British Railways as "accommodation grades".

Table 11 gives further information on the grades which receive workers transferred on grounds of ill health. The "accommodation" rate of the receiving grades has been calculated by taking the total number of people entering as a percentage of the number already in the grade.

TABLE 11
RECEIVING GRADES

	Accommodation Rate	Rank Order by Mean Age	Rank Order by Average Duration per Person
1. Shedman	2·7	15	3
2. Goods porter	2·3	15	5
3. Stores issuer	0·7	10	6
4. Clerk	0·3	24	7
5. Workshop labourer	0·3	14	4
6. Yard inspector	0·08	1	2
7. Shunter	0·002	25	9

Shedmen and goods porters are frequently used as receiving grades and they may be considered to be "accommodation" receiving grades, while the others, although receiving some transfers, cannot really be so regarded.

A notable characteristic of all these grades is that they are "sick" grades comprising seven of the nine grades within the highest third on average duration per person rate. It is thus probable that not only do they retain their own sick men, but they accept sick workers from other grades less able to tolerate sickness absences. These grades will therefore be selected for further detailed study in the follow-up survey.

From the data at present available to us there does not seem to be an age trend in the job changes due to sickness.

More Suitable Grades for Older Workers.—Certain grades may be more suitable for older workers. We have conducted a detailed age analysis of the railway research population (see Gordon, Emerson, and Pugh, 1959) and on this basis tentatively identified four grades as being possibly more suitable for older workers in view of their high age distribution. These were timekeeper, luggage room attendant, stores issuer, and shop officeman. The fact that the mean age of men in a particular occupation is high does not of itself imply that it is a more suitable occupation for older workers, but it does at least indicate that such jobs are being "held down" by them. It is obviously relevant to consider the sickness absence experience of these particular grades.

The grade of shop officeman is the only one of the four which lies in the "sick-sick" quadrant of Table 8. It provides sedentary routine work in which little or no initiative is required (Table 1, No. 18). If it is a "sick" grade because it retains its own sick members and absorbs others, it would be expected to show up as one of the grades to which people are transferred. In fact this is not the case from our own data. We cannot, on this basis alone, reject the possibility of it doing so, for on our returns covering one year the numbers transferred are small and the grade consists of only 100 people. There may have been no vacancies in this grade during the period of study; for example, the grade may have received too extensively during the preceding period. Clearly the grade of shop officeman must be investigated further.

Stores issuer and timekeeper fall into different squares from one another (Table 8), but both are adjacent to the "sick-sick" quadrant. Stores issuer also ranks high on the average duration per person measure and is shown to be a grade into which people are transferred on account of sickness. Timekeeper has no people transferred to it, but it is a small grade and so might not show the effect over the period concerned. Luggage room attendant is a complete anomaly, since it has a very high duration per episode and a very low sick person rate. It has the lowest average duration per person.

One of the outstanding features of the railway research population is the very large size of the operating grades, the footplatemen and the signalmen, and the very small size of what we have tentatively identified as grades into which they might transfer. Provision for the large number of older workers would indeed present many difficulties. It should not be concluded that our account covers all the provision that is made. The present examination has not encompassed changes within the existing grades; for example, whether and in what state of health locomotive drivers are transferred from the more strenuous to the less strenuous, or from the more responsible to the less responsible, runs. This further information is not available from our present records.

Discussion and Conclusions

Certain main points may be made on the basis of the data which have been presented.

When sheer number of episodes is the criterion of the amount of sickness absence, the railway research population compares favourably with other populations studied. On the other hand, when duration per episode is the index, the railway research population shows a higher figure at all ages than the only other population with which we have been able to compare it. It may well be that the greater tendency to long durations of sickness in the railway research population is due to the type of working conditions.

This view is supported by our analysis of age standardized rates for the various grades, and of the relation of sickness absence patterns to responsibility and conditions of work. On the first point, we conclude that the differences due to grades are at least as striking as those due to age; on the second, that duration of sickness episode is greatest where exposure to the weather is greatest. Examination of Table 1 shows that 13 grades (representing 7,520 men) are classed as exposed to the weather, compared with 14 grades (representing 6,554 men) which are classed as sheltered from the weather. A comparison of the corresponding proportions in the London Transport population would help in elucidating this point. As far as the railway research population is concerned, a much closer examination of the conditions of work, psychological no less than physical, is required.

Closely related is the negative correlation we have reported between the sick person rate and the duration per episode for the various grades. Our conclusion is that a grade has either a comparatively large number of people with short sickness episodes, or a smaller number of people with comparatively longer episodes. Some preliminary analysis of the kind of variables which may underlie this state of affairs has been carried out. But again, a much more detailed analysis, especially of the psychological aspects of the work involved in each grade, is required before the reasons for this observation can be elucidated.

The exclusion of the uncertified episodes has the effect of drastically reducing this correlation. Some data bearing on this point will be presented in a later report. The possible implications of the uncertified sickness data are discussed below.

The sickness pattern of the age groups is similar in form to that commonly found, namely, that in the older age groups the episode rates tend to be only slightly higher than at younger age groups, but that the episodes of the older men tend to be longer. Here too, considerable amplification is necessary. A first step would be the examination of the age distributions for the diagnoses recorded at the time of the sickness episode. The direction of subsequent investigation would depend on the nature of these distributions, but ultimately an analysis of the whole question of sickness thresholds and the complex of pressures effective at the onset, during, and at the end of an episode would be required.

The pattern resulting when our five types of sickness duration are analysed by day of starting sickness lends itself to interpretation in terms of "morale". Such an interpretation has been discussed, but it is, in effect, a series of hypotheses, all of which need to be tested by psycho-social investigations. In examining what happens when a man takes sick leave, it is important to consider not only the nature of his sickness, his working conditions, and his general attitude to his job, but also the nature of family pressures to remain at work, loyalty to the working group, and other factors. In the main, our data at present are consistent with an interpretation that for whatever reason, men who will eventually take sick leave, often for a longer period, do attempt to carry on working to the end of the week in which they first begin to feel ill.

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THE ACTION EXERTED BY CERTAIN PNEUMOCONIOTIC FACTORS UPON THE ACID MUCOPOLYSACCHARIDE CONTENTS OF PULMONARY MACROPHAGES

BY

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Experimental inhalations of silicon dioxide and tobacco smoke cause a gradual increase in the number of pulmonary macrophages containing metachromatic material within the nucleus and cytoplasm, and they may assume the appearance of mast cells. Many pulmonary macrophages containing metachromatic material were found in anthracotic human lungs.

Histochemical techniques identify this material as acid mucopolysaccharides. After a more prolonged action of pneumoconiotic substances, mucopolysaccharides disappear after hyaluronidase extraction.

On the basis of these findings the increased amount of acid mucopolysaccharides in the connective interstices of the lung during the phase preceding the onset of fibrous lesions is explained by the prolonged irritative action of pneumoconiotic substances, which are believed to determine hypersecretion of acid mucopolysaccharides by the pulmonary macrophages.

In studying the histochemical features of the experimental process of pneumoconiotic fibrosis of the lungs (Lupu, Velican, Gociu, and Racoveanu, 1958), we found that during the phase which precedes the appearance of fibrous lesions metachromatic and P.A.S.-positive material accumulates in the connective interstices of the lung, disappearing almost completely after hyaluronidase extraction. It seems to play an important part in the development of fibrosis, as it is within this mass that precollagen fibres appear. We therefore attempted to learn whether the mucopolysaccharidic substance is secreted by pulmonary macrophages, and to this end investigated this process under conditions of hypersecretion by subjecting the reticular cells of the lung to the irritative effect of certain fibrogenic dusts, *i.e.*, precisely those agents which in the long run determine the accumulation of acid mucopolysaccharides within the connective interstices of the lung.

We have not encountered any similar investigations in the available literature.

Material and Method

Experiments were carried out on 60 guinea-pigs, divided into two groups each of 30 animals.

The first group was exposed for four hours in a dusting room in which pure silicon dioxide was dispersed in a concentration of 15 mg./cu.m.; the most frequent (90%) particle size was 1-3 microns. Small groups of six animals were killed at various intervals after being removed from the dust (Table 1).

The other group was subjected to daily inhalations of tobacco smoke, each inhalation lasting 30 minutes. Groups of six animals were killed at one hour after the first inhalation, then after two, four, six, and 15 inhalations (Table 2).

Observations were also made in human subjects by the post-mortem collection of lungs displaying various degrees of anthracosis.

Smears were made from all the collected lungs and stained with toluidine blue, May Grünwald-Giemsa, methylene blue, Hotchkiss-McManus stain, and Best carmine stain. Enzymatic extraction techniques, using testicular hyaluronidase for 15 to 30 minutes at 37° C., were applied, and the same cells were studied in comparative photomicrographs before and after being subjected to the action of the enzyme. As a control test, one half of each slide was subjected to inactivated hyaluronidase. "Pneumograms" were made of the smears from each of the lungs examined by counting 500 pulmonary macrophages, and obtaining the percentage of cells showing metachromatic granules.

Results

" Pneumograms " on normal guinea-pigs after staining with toluidine blue showed pulmonary macrophages containing slightly metachromatic granules, the percentage varying from 0 to 2. In the normal human lung this proportion is 5 to 6%. The percentages of cells containing metachromatic material after the inhalation of silicon dioxide and inhalations of tobacco smoke are given in Tables 1 and 2. The human anthracotic lung showed areas in which the pulmonary macrophages contain mucopolysaccharides in a proportion ranging from 35 to 82%.

TABLE 1

ONE EXPOSURE TO SILICON DIOXIDE DUST (EXPERIMENT 1)

No. of Animals	Interval (in hours) at which Animals were Killed after Removal from Dust	Pulmonary Macrophages Showing Metachromatic Granules (%)
6	24	4
6	48	6
6	72	10
6	90	13
6	120	14

TABLE 2

DAILY INHALATIONS OF TOBACCO SMOKE (EXPERIMENT 2)

No. of Animals	No. of Inhalations before Sacrificing Animals	Pulmonary Macrophages Showing Metachromatic Granules (%)
6	1	8
6	2	14
6	4	18
6	6	21
6	15	24

Metachromatic material appeared both in cells containing inclusions and in those which harboured no foreign bodies within the nucleus and cytoplasm. There seems to be no direct relationship between the number of phagocytosed particles and the amount of metachromatic material detected in the respective cell; on the contrary, this material was more abundant within the cells containing some or few inclusions.

Such observations cannot be recorded as clearly in sections because the acid mucopolysaccharides in each cell are partially or wholly removed by the microscopic techniques.

As regards the intracellular pattern formed by the metachromatic material, the following aspects are more characteristic: The substance may be spread diffusely or in the shape of granules, both in the nucleus and in the protoplasm (Fig. 1). In some of the cells, all of the metachromatic material was concentrated in the nucleus, which appears as an intensely metachromatic spot, without any visible structure (Fig. 2). In other cells it was exclusively located in the protoplasm in the shape of small pulverous granules displaying low or moderate metachromasia (α and β metachromasia according to Pearse's classification), sometimes assuming a mast cell appearance. In other cells, the metachromatic material was seen both in the nuclei and in the cytoplasm. In the nuclei it seemed to be concentrated most frequently within the nucleolus or around it and around the nuclear membrane. In the cytoplasm it surrounded the nucleus and especially the intracytoplasmic inclusions (Fig. 3).

As regards the cytochemical characteristics, these substances are soluble in water on unfixed material. After toluidine blue staining, decolorizing, washing with water and restaining by the same stain, they disappear almost completely. This is why previous fixation by absolute alcohol is necessary for the study of the enzymatic action. The Hotchkiss-McManus reaction was strongly positive; in the same cell its intensity sometimes exceeded that of the area of metachromatic reaction, both in the nucleus and in the cytoplasm (Fig. 4). Best carmine staining yielded negative results.

Testicular hyaluronidase extraction was constantly negative or uncertain in animals killed shortly after the inhalation of tobacco smoke or silicon dioxide. In smears of human anthracotic lungs we could see that after extraction the metachromatic material had entirely disappeared in most of the macrophages investigated both before and after enzymatic action (Fig. 5), but in those cells in which mucopolysaccharide films were present around coal inclusions, enzymatic extractions generally failed to bring about changes.

Discussion

The results obtained with " pneumograms " and hyaluronidase extractions showed that after the action of certain pneumoconiotic factors the amount of acid mucopolysaccharides contained in pulmonary macrophages is significantly increased, as may be shown by ordinary histochemical tests.

During the initial phase of the appearance of these substances, they are not extractable by testicular hyaluronidase; this may prove that neither hyaluronic acid nor chondroitin sulphuric acid contribute to their formation during this period. At a more advanced stage, the amount of metachromatic material elaborated by pulmonary macrophages increases, and at the same time its chemical composition seems to change, when it is partially formed of the above-mentioned acids as well as by

FIG. 1.—Macrophage in a pulmonary smear from animals subjected to five inhalations of tobacco smoke. A vesicle may be seen in the nucleus, containing a globule of intensely metachromatic material. It is surrounded by a diffuse intranuclear agglomeration of the same substance. Toluidine blue × 3,000.

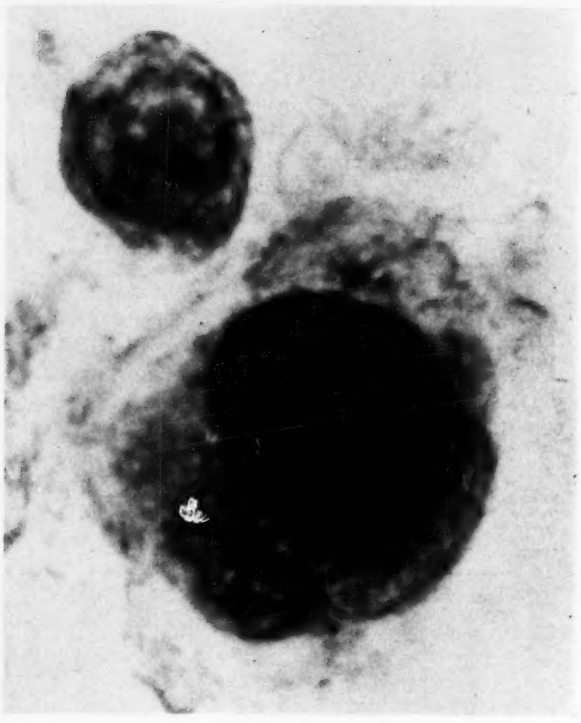


FIG. 2.—Macrophage in a lung section from animals subjected to a single inhalation of silicon dioxide and sacrificed 120 hours later. The whole nucleus displays intense and diffuse metachromasia. Toluidine blue × 3,000.

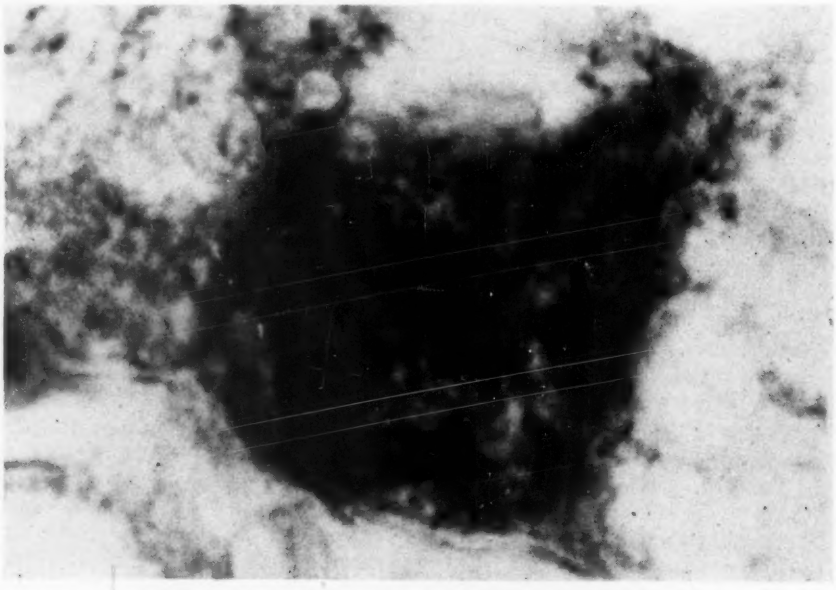


FIG. 3.—Macrophage in a lung section from animals subjected to 15 inhalations of tobacco smoke. Considerable amounts of intranuclear and intracytoplasmic metachromatic material may be seen, especially around the nucleus. Toluidine blue × 3,000.

FIG. 4.—Macrophage in a lung section from animals subjected to 15 inhalations of tobacco smoke.

(*a*) The nucleus is intensely and diffusely metachromatic. The cytoplasm is likewise diffusely, but less intensely metachromatic.
Toluidine blue × 2,000.

(*b*) The same cell after P.A.S. staining. Both the nucleus and the entire cytoplasm are intensely and diffusely stained.
Hotchkiss-McManus stain × 2,000.

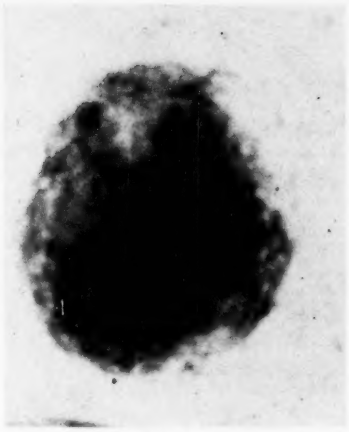
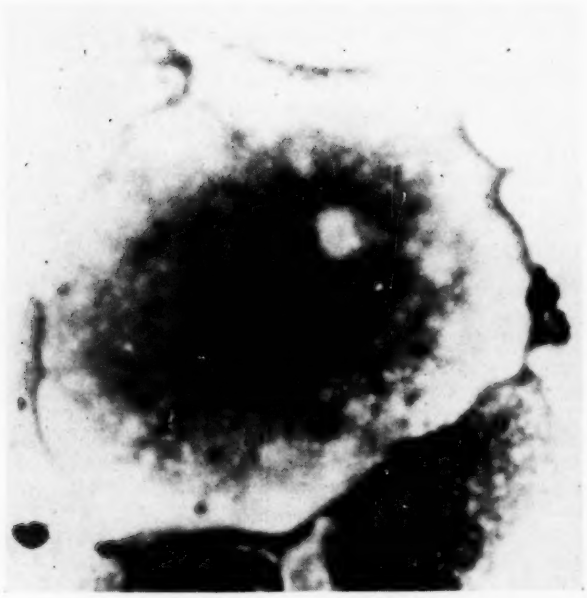


FIG 4 *a*.

FIG. 4 *b*



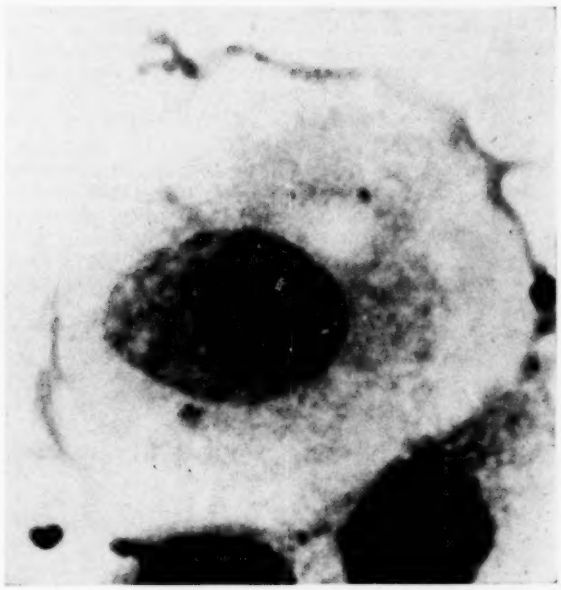


FIG. 5.—Human pulmonary macrophage in a smear from a case of anthracosis

(*a*) The nucleus is covered by a slightly metachromatic substance.

(*b*) After hyaluronidase extraction this substance disappears altogether. Toluidine blue stain, hyaluronidase extraction, and restaining with toluidine blue. × 3,500.

hyaluronidase extractions performed in preparations of human lungs with anthracosis.

Our investigations justify relating the appearance of acid mucopolysaccharide substances in pulmonary macrophages immediately after the action of certain pneumoconiotic agents to the massive increase of these substances in the connective interstices of the lung during the periods preceding the development of the fibrous process. This accumulation of metachromatic material appears to be the result of an exaggerated secretion of the pulmonary macrophages as a result of the prolonged action of pneumoconiotic factors.

The results of our study do not support the hypothesis concerning the secretion of acid mucopolysaccharides by fibroblasts (Burkl, 1952; Wirtschafter, 1957), *i.e.*, by the same elements which are supposed to participate in the formation of collagen fibres. In the normal guinea-pig lung, as in the one subjected to the brief action of pneumoconiotic factors, no such cells can be demonstrated and the data resulting from the present note solely concern elements of the reticulo-histiocytic type.

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MISCELLANEA

A Case of Cirrhosis and Primary Carcinoma of the Liver in Chronic Industrial Arsenical Intoxication

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A case of primary liver carcinoma associated with liver cirrhosis in a man who had handled arsenious oxide and sodium arsenite for over 20 years is described with reference to his occupational history, clinical condition, and with details of pathological findings.

Arsenical poisoning may occur in industry, in three forms: (1) From inhalation of or contact with dust of inorganic compounds, (2) from inhalation of arseniuretted hydrogen, (3) from contact with organic arsenic compounds. The inorganic compounds act as local irritants to the skin and mucosa and may have a carcinogenic effect. Arseniuretted hydrogen acts as a haemolytic agent and organic arsenic compounds as vesicants. The hepatotoxic action of inorganic arsenic compounds such as potassium arsenite, which is contained in Fowler's solution, has long been recognized by those using this solution as a therapeutic agent but has been scarcely mentioned as an industrial hazard. Skin cancer constitutes a well recognized occupational hazard.

The occurrence of hydrops and ascites following the ingestion of arsenic was first recorded by Bang in 1774. Hutchinson (1895) was apparently the first to report that cirrhosis and ascites can be due to prolonged administration of arsenic and to draw attention to its carcinogenic properties. Since then, many cases suggesting arsenic as an aetiological agent in cirrhosis of the liver have been published. It is almost disregarded today when considering the aetiology of portal cirrhosis.

Case Report

A.T., aged 46, was first admitted on November 18, 1950. His work had entailed contact with an inorganic arsenic compound (sodium arsenite) for about 18 years. He was employed on different parts of the process from time to time and finally was the foreman in charge of the arsenic plant. The process consists of mixing white arsenic (arsenious oxide) with soda-ash (crude sodium bicarbonate) in a heated bath of water. The solution is pumped to a concentration tank where it is highly concentrated by heat. The liquor from this tank passes into a reverberating furnace where it is dried to form lumps of sodium arsenite. This is raked from the furnace into a barrow. The lumps are then ground in a mill to a fine powder and mixed with methylene blue. There are usually three men employed: one shovels white arsenic and soda-ash into the tank, the second is in charge of the furnace and rakes the material when it is dry, and the third is in charge of the grinding mill and fills the drums with the finished product. A.T. was employed in any of these processes. The men usually wore protective masks of unknown design and gloves. His alcohol consumption was an occasional pint of beer and, rarely, spirits.

Ten days before his admission he had pneumonia and while he was recovering he noticed rapidly increasing, painless, abdominal swelling. There was no significant previous history. He was afebrile (pulse 90 min., regular, B.P. 130/80 mm. Hg). There was no oedema of the feet. The tongue was coated and the throat congested. The abdomen was tense and uniformly distended with fluid. Superficial abdominal veins were dilated. Palpation of viscera was not possible. Other systems revealed nothing abnormal. The urine contained no albumin or sugar. Blood examination showed Hb 100%, erythrocytes 5 million/c.mm.; leucocytes 7,000 (normal differential count) and E.S.R. 8 mm./hour. The ascitic fluid had a specific gravity of 1020, proteins 6%, a few lymphocytes, no malignant cells, and was negative in culture. Plasma proteins were 6·48 g. %. A chest radiograph on November 20, 1950, showed elevation of both domes of the diaphragm but no focal lesion. A 24-hour specimen of urine examined by the Forensic Science Laboratory, Preston, contained 0·13 mg. of arsenious oxide (equivalent to 0·86 p.p.m. arsenious oxide).

He was treated with a low-salt diet, mercurial diuretics, streptomycin, and paracenteses. He was discharged on January 2, 1951, and returned to his work with arsenic.

He was well until February 13, 1956, when he was re-admitted on account of acute abdominal pain and vomiting of one day's duration. Exploratory laparotomy revealed enormously thickened parietal peritoneum, adherent coils of bowel, and cirrhosis of the liver. Post-operative chest radiographs showed migratory pneumonia and he was treated with penicillin and streptomycin. He was discharged on February 28, but did not return to work.

Seven days before his last admission on October 3, 1957, he noticed puffiness of the face and rapidly increasing swelling of the abdomen. There was no history of haematemesis, jaundice, or bleeding per rectum. He was pale, oedematous, and puffy. The skin showed mottled brownish pigmentation, chiefly in covered areas. The skin of the palms and soles was markedly thickened. He was afebrile (pulse 90 min., B.P. 120/80 mm. Hg.). The abdomen was very tense and swollen with fluid, but there was no fluid thrill or shifting dullness. Superficial abdominal veins were engorged and visible. Viscera were not palpable. Rectal and proctoscopic examina-

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tions revealed no abnormality. Other systems were normal.

The urine contained no albumin or sugar. A blood examination showed Hb 78%; leucocytes 8,700 c.mm. (normal differential count), E.S.R. 4 mm./hour, total serum proteins 4·9 g. % (albumin 2·3 g. %; globulin, 2·6 g. %) and urea 48 mg. %. Liver function test results were: alkaline phosphatase 10 units, thymol turbidity, 1 unit, zinc turbidity 5 units, serum bilirubin 0·7 mg. %, direct and indirect Van den Bergh tests negative. Ascitic fluid: sp. gr. 1030, proteins 8·28 g. %, mesothelial cells and few polymorphs, no malignant cells, culture negative. Blood group A rhesus negative. Serum chlorides 94 mEq. per litre; sodium 128 mEq. per litre; potassium 3·9 mEq. per litre. A chest radiograph showed loss of translucency at the right base, suggesting a recent inflammatory lesion. A cardiovascular outline was within normal limits; the oesophagus showed evidence of varicosities.

The Forensic Science Laboratory, Preston, reported as follows:

A. Hair, total weight 0·1379 g., 209 p.p.m. of arsenious oxide
B. Nail clippings, total weight 0·0390 g., 564 p.p.m. of arsenious oxide
C. Skin biopsy, total weight 0·1402 g. Arsenic not detected.

He was treated with a low-salt diet, mercurial diuretics, and parenteral vitamins, but the oedema gradually increased. Twelve days after admission he developed vertigo and became apathetic, disorientated, and confused. Flapping tremors were detected once. He was put on a "liver failure régime" but his condition gradually deteriorated, and he became deeply comatose. On October 19 he had two haematemeses (about 2 to 4 oz.), Next day he developed pulmonary oedema and died.

Necropsy Report

Dr. R. D. Popham reported as follows: "Body of a male aged about 45 years. He was well nourished with gross oedema of the trunk and legs and a distended abdomen. Rigor mortis was absent. There was marked hypostatic cyanosis. The surface of the body showed blotchy, greyish-brown pigmentation of the skin of the trunk, upper arms, and legs. There were many small spider naevi and hyperkeratotic thickening of the skin of the hands and feet. There was a healed left paramedian surgical incision. No other scars or injuries were detected. The pericardium was normal. The heart was normal in size and weighed 300 g. The myocardium was flabby and pale but there was no hypertrophy or infarction. The foramen ovale was closed and all valves were normal. There was slight atheroma of the aorta and coronary arteries. A partly thickened thrombus was present in the splenic vein. The pleural cavities were obliterated by thick fibrous adhesions. Both lungs weighed approximately 800 g. and showed some emphysema with slight oedema and gross venous congestion. There was thickening of the parietal and visceral peritoneum and the whole of the intestine formed a mass bound together by dense fibrous adhesions. This mass was adherent to the other viscera. The liver, spleen, and stomach were covered by thick peritoneum of the "sugar icing" type. The liver weighed 1,400 g. Its capsule was smooth and thickened as above. The cut surfaces showed very little remaining liver tissue, its place being taken by multiple nodules of varying size of white carcinomatous tissue. The liver tissue seen was fibrous. The spleen was congested and fibrous and weighed 400 g. The pancreas was normal. The stomach contained fresh and altered blood. Three flat superficial ulcers, each about 1 cm. diameter, were present on the posterior wall. Varices of gastric and oesophageal veins were present. The intestines were slightly distended but there was no obstruction. The small intestine contained altered blood. The mesenteric glands were normal, except for one small calcified gland. The generative organs were normal and the prostate was not enlarged. The capsules of the kidneys were not adherent and both renal cortex and medulla were normal. The suprarenals were normal. The brain weighed 1,300 g. and showed slight venous congestion. The cause of death was haemorrhage from oesophageal varices, and primary carcinoma of the liver with plastic peritonitis. The histopathological section of liver confirmed the diagnosis of cirrhosis with primary carcinoma."

Discussion

Although arsenic is commonly met with in industry only eight cases of chronic arsenical poisoning were reported during the years 1950 to 1954 (Chief Inspector of Factories, 1955).

Arsenic determinations on normal human urine are quoted by Cox (1925) as varying between 0 and 0·7 mg. of arsenious oxide per litre, the commonest figures being 0·0 to 0·2 mg. per litre. More recently, Sultzaberger (1943) reported values of about 0·03 mg. per litre and Kingsley and Schaffert (1951) quoted a range between 0·046 and 0·206 mg. per litre. The results of the radioactivation method carried out by Smales and Page (1952) showed a range from 0·013 to 0·33 mg. of arsenic per kg. of urine, which is within the range quoted by Cox. There are many reports on the arsenic content of hair. For example, Szép (1940) examined hair and nail clippings and found that normal "healthy" levels were for hair, 0·27 to 0·77 p.p.m. and for nails, 1·5 to 5·2 p.p.m. Künkele (1940) considered that indications of arsenical poisoning were given by contents greater than 3 p.p.m. in head hair and 0·1 mg. per litre in the urine; results by the radioactivation method ranged from 0·51 to 2·1 p.p.m. for hair, from 0·82 to 3·5 for finger nails, and 0·52 to 5·6 p.p.m. for toe nails. A new modified method of polarographic estimation of arsenic in blood and urine was introduced by Naoyoshi, Norifusa Iwataki, and Toshikazu Yamamoto (1955) who found that the minimum amount of arsenic detectable was 0·5 γ. A normal Japanese adult had 0 to 11·4 γ of arsenic per 100 g. of blood and 0 to 28 γ per litre of urine, while workers in the arsenic industry were found to have 9·2 to 20·8 γ and 82 to 113 γ respectively.

The figures obtained in the case now reported were extremely high compared with "normal" arsenic levels and even with those published for workers in the arsenic industry. It is possible that "mechanically bound"

arsenic, that is, on the surface of the hair and nail, was present.

Parker (1957) showed by analysing the necropsy findings that malignant change complicates cirrhosis oftener than is generally appreciated, particularly in the male. It has also been suggested by Sommers and McManus (1953) that multiple internal carcinomata may develop in chronic arsenical poisoning.

The clinical picture and positive laboratory findings showed that this patient was suffering from chronic arsenical poisoning. In the absence of other aetiological factors, arsenic appears to have been the cause of cirrhosis-carcinoma of liver.

I wish to express my thanks to Dr. W. A. L. MacFadyen for allowing me to publish this case report and for valuable criticism; Dr. R. D. Popham for the necropsy report; Dr. W. B. Waring for his help; Col. Backhouse, H.M. Coroner, for permission to publish the necropsy report, and to Miss M. Crabtree for secretarial help.

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BOOK REVIEWS

Le Otopatie da Rumore e Nozioni di Audiologia. By Vittorino Pescetti. (Pp. xii = 96; 17 figures. Lire 1,200.-.) Rome: Edizioni E.N.P.I. 1956.

This volume is No. 9 of a series of monographs on various aspects of the prevention of accidents and diseases in industry. It is published by the E.N.P.I. (National Organization for the Prevention of Accidents), a body concerned with industrial health services as well as accident prevention which makes available to industry all that we understand by these terms as well as specialist service in respect of any aspect of them. The E.N.P.I. is, in conception, a private, non-profit making concern, but has, in fact, become a para-state service with centres in Rome, Milan, Turin, and elsewhere. Its services include all aspects of safety organization, medical examination of workers, records, analysis of environmental contaminants, etc., which are paid for by industrial concerns on a per capita basis or some other arrangement. Its great advantage to the industrialist is that he simply hands over his problem to E.N.P.I. and need not bother about it any more unless a recommendation for improvement or change of plant, process, or environment, is sent to him. E.N.P.I. obtains doctors for industry and facilitates their operation.

Among its many activities the E.N.P.I. includes the publication of safety literature and posters, together with reviews of medical and safety subjects and monographs on specialized aspects of industrial medicine. By means of lectures, demonstrations, exhibitions, and symposia it maintains valuable contact and cooperation between state authorities, workers' organizations, medical associations, universities, and employers on manifold aspects of occupational health and safety.

The volume under review bears, to one who is acquainted with many of the personnel and methods of E.N.P.I., the stamp of that organization in that it embodies, with characteristic lack of prolixity, the fundamental and practical principles of audiometry and the pathology of noise as these affect or enter into the field of industrial medicine. It demonstrates the need in our work for monographs, of text-books not in the traditional model but consisting of groups of quasi-monographs.

We are not fully informed on the activities of industrial medical officers in this country in the field of measurement and control of noise in industry. The subject does not figure notably in our journals. In the U.S.A. and some European countries there is great interest in this field, and not only in those trades which are outstandingly noisy (boiler makers, metal workers, riveters, engine testers, aircraft mechanics, nail makers, users of pneumatic hammers, and others) but also in trades or jobs where it is not intensity (energy of sound measured in decibels) and frequency (number of cycles per unit time) or long-acting dissonances of high intensities but rather

noises of moderate intensity and frequency which come to bear on workpeople for many hours a week for years. Examples are airmen, millers, textile workers, mechanized office workers, power-house workers, and bus drivers. The problem here is, of course, not one of the development of cochlear lesions but of more subtle effects which may rebound on social, technical, economic or even political aspects of society. Some investigator, requoted by Pescetti, finds that a diminution of noise leads to better production and fewer errors in typing and calculating machine work; others describe an adverse effect on operations requiring concentration whereas work on a noisy spinning mill was not affected.

There is much to commend Pescetti's view that more investigations are called for in the realm of psychomotor, psychological, and neuro-vegetative reactivity to sound, especially having regard to the great variability of human subjects in these respects. This variability is found more obviously in workers who are exposed to injurious noises during their work. Pescetti, when testing at 2,000 cycles per second, gives illuminating figures for such workers between 20 and 40 years of age in Italy: For periods up to five years in such work, 25% show hearing losses from 20% to 40%; for periods from five to 10 years in such work, 35% show hearing losses from 30% to 50%; and for periods from 10 to 15 years in such work, 50% show hearing losses from 40% to 70%. The fact that workers may be unaware of hearing loss and that older workers are more likely to develop such loss necessitates routine audiometric tests as a control and removal of affected or susceptible men from work which is inimical to them.

The tendency to attribute loss of auditory sense to working conditions has led to the introduction of tests to detect simulation and to eliminate cases due to causes, such as age (higher frequencies), infection, chemicals (CS_2, quinine), cocaine, tobacco, alcohol, etc., other than industrial noise. The objective and subtle audiometric tests shortly presented by the author are well worth study (chapter 7) although the possibility of outsmarting the examiner is not negligible.

On the difficult engineering problem of prevention of noise in industry, the author offers a number of well-recognized means, for example, isolation of noisy machinery, remote control, better lubrication and maintenance, raising machinery from floors on badly conducting material, elimination of high-frequency noises by diminishing the r.p.m. of motors, elimination of echoes and resonance from walls, as well as the use of sound-absorbing materials.

The use of ear plugs must be considered when external control is impossible, and is not always acceptable to the worker, but is made more acceptable if a measure of sound (say 20 to 30 decibels of amplitude) is allowed to enter thus precluding total auditory isolation during sustained work. But no such consideration should enter if very high intensities or frequencies are likely or if the subject is a susceptible, for here the danger of irreversible damage is too great.

Much other interesting and very readable information is given in this little volume. The frequent continental habit of referring to authors without giving the reference is a nuisance which Pescetti has not eliminated. We recommend that an English translation be made; it would be a very useful, rapid review of this most important subject.

M. W. GOLDBLATT

Report on the Health of the Army 1954. W.O. Code No. 11709 - 24/General/3926. (Pp. 180 roneod). London: H.M. Stationery Office. 1958.

This report shows the steady progress made in the prevention and treatment of disease in the Army and the comprehensive nature of the service provided for the soldier and his family both at home and overseas.

Apart from the statistical tables and notes, a large part of the text is devoted to prevention (Army health), but the work of the hospitals and pathological department is also amply covered.

In a short review no detailed analysis is possible, but the high standard of medical practice in the Army is reflected in the admission rates to medical units which are generally, and in many cases greatly, lower than in previous years. It is clear that the excellent work carried out on the preventive side has, to some extent, changed the pattern of disease incidence in recent years, and the risks to which the soldier and his family are exposed while serving overseas. Perhaps the most striking example of this is the fall in admissions for skin complaints in the Middle East Command, where the rates for septic skin conditions have hitherto been high. The investigations carried out in 1951/52, and the recommendations contained in the Squire Report have evidently borne fruit.

The assessment of recruits by Ministry of Labour and National Service Medical Boards was generally satisfactory; 85% were examined by mass miniature radiography before acceptance for service. The remaining 15% were radiographed during the first week of service, and a number were then found to be suffering from tuberculosis which increased the sickness rate for this disease in the under-20 age group. Table 20 lists the causes of discharges during the first week of a man's service and just over 50% of discharges were due to psychiatric, eye, and ear conditions. Attention is drawn in the text to the method of discharge under Queen's Regulations (1955), and a distinction is made between those who were unfit on medical grounds and those who failed to reach the required Pulheems standard for employment in the Army. This latter group was discharged administratively.

While there was little change in the discharge rate for 1954 compared with 1953, there were 50% more administrative discharges. This would appear to indicate a raising of the retention standard, and the fact that the incidence of dullards among regular recruits is higher than among National Servicemen suggests that many of these young men seek to join the Army as a last resort. The excellent results obtained at the physical development centres should be noted. In Southern Command alone, of 1,870 attendances, 1,407 attained the required standard and a further 427 were borderline cases fit for service in any part of the world. This is worthwhile work from the national point of view as well as the Army angle.

Under the heading "Personnel Research" a wide variety of subjects are dealt with, most of which are of particular interest to the Service; but the value of the nation in relation to the training and work of the soldier,

investigated by a team under the general direction of the Medical Research Council, is of general interest and has wider application. Research into the wastage and spoiling of food by insects, carried out at the Royal Army Medical College, Millbank, is also of general interest.

Up to the time of evacuation of British Forces from the Canal Zone, the prevention of enteric remained a problem, for, although only four of the 217 cases admitted to hospital were due to typhoid fever (the remainder being paratyphoid B), the enteric investigation team failed to identify either the source or vehicle(s) of infection. Nor did they discover the reason for the high incidence of enteric in the Canal Zone. However, certain recommendations for reducing incidence are made, including sterilization of cutlery and crockery immediately before meals instead of after meals.

Attention is drawn in the Report to the ever present risk of water-borne illness in the absence of controlled bulk supplies and to the introduction of a fixed dose chlorination of water supplies in the field. The well-known Horrocks test for estimating chlorine dosage is being replaced by the Elliot neutral red test.

A. N. B. ODBERT

Safety Techniques for Radioactive Tracers. By J. C. Boursnell. (Pp. xii + 68; illustrated. 7*s*. 6*d*.) Cambridge University Press, London. 1958.

This short book is mainly directed to laboratory workers using radioactive isotopes as experimental tracers ("open" sources) and contains much useful information on handling such radioactive materials and keeping workers and working areas clean and safe. The only common danger not mentioned is the possibility of dispersion by boiling when a recalcitrant ampoule of concentrated solution is finally opened after being heated up by repeated application of a hot glass bead or wire (p. 27). The hazards of "spray" are probably not emphasized sufficiently: whenever liquid drops are made, as in almost any operation involving transfer of liquids, microdrops are also formed which drift away in the air to be inhaled by the worker. Such personal contamination is unavoidable without the use of totally enclosed and individually ventilated work spaces (*cf.* p.11), but is often of no practical importance. The book does not deal with the handling of radio-isotopes in the "sealed" form such as the thickness gauges or radiographic sources used in industry, where the amount of radioactivity is much greater than with "open" sources and the hazards generally present themselves in a different way.

Dr. Boursnell has attempted one of the most difficult of all tasks for an author, a short summary of a new technical field which shall be accurate, sufficiently explanatory, and intelligible without misunderstanding. One fault, not altogether avoided, is the imprecise general statement, *e.g.*, that film badges are essential except when soft β-emitters are employed (what is the precise dividing line?), or that prior permission is needed from the relevant departments of the local authorities before putting any quantity of radioactive materials into drains (which are relevant?), or that animal carcases can be incinerated in the normal way when their radioactivity has decayed to a low level (not further specified). There is also some looseness in the general arrangement which can be important in a book without an index, *e.g.*, the general necessity of "dummy" runs to test the safety of a proposed procedure before actually using radioactive material is discussed in the section on contamination by inhalation.

Few errors of fact were noted. It is not true that the lens of the eye is particularly susceptible to damage by all forms of radiation, only by neutrons which are not in fact given off by radio-isotopes. It is also not true that the first sign of over-exposure of the whole body to radiation is a fall in the blood leucocyte level, and it is regrettable that continued support is given to the recommendation that workers with tracer quantities of radio-isotopes need regular blood counting. On p. 40, α- is a misprint for γ-. The headings of the columns giving the maximum permissible concentrations of radio-isotopes in water and air (Appendix III) would be less ambiguous if the multiplying factors, *e.g.*, 10^7, were included in the brackets. There may be good administrative reasons for insisting that film badges should be worn in a conspicuous place but it seems illogical to write that they must not be kept in the pocket where they may be screened by the material of the coat if, in fact, their purpose is to measure the dose received by the clothed body. On general biological grounds the inside of a trouser pocket might well be a better place for a film badge than the outside of a breast pocket.

In Appendix III the recommendations on disposal of radioactive waste seemed to err on the side of over-caution. The figures strongly suggested as upper limits for the amount of radioactivity it is safe to dispose of daily (p. 46) are roughly one hundred times less than those given in the tables and derived from accepted maximum permissible levels for continuous exposure for the duration of a working life time. The generally accepted principle that prolonged exposure of a large population should be at a lower level than of those occupationally exposed is a bad argument for justifying a marked reduction below maximum permissible levels when disposing of waste. These levels are derived on the assumption of continuous complete immersion in sewage or the regular daily ingestion of 1½ litres. There is thus a large margin of safety provided for the general public in the circumstance that exposure to radioactive sewage is accidental, uncommon, and nearly always very temporary. It is disappointing to have to make this criticism of a book which in many respects fulfils its aim of providing a sane and reliable guide to the beginner.

R. H. MOLE

The Physical Treatment of Varicose Ulcers. By R. Rowden Foote. (Pp. 125; 88 figures. 15*s*.) Edinburgh and London: E. & S. Livingstone. 1958

In this clearly written and well illustrated book Rowden Foote deals comprehensively with the conservative treatment of leg ulcers and varicose veins.

He estimates that there are a quarter of a million sufferers from these complaints and makes the point that hospital beds to treat these conditions are scarce and expensive. In many cases cure can be effected as an out-patient and even where surgical procedures such as

tying and stripping veins are to be performed, preliminary treatment is desirable.

The techniques described in this book are divided into two parts, (1) nursing care and (2) physiotherapeutic measures.

Nursing care is concerned with pressure bandaging to reduce oedema and compress the ulcerated area. A full description is given of the types of bandage available and the correct method of application. In these pages there is a wealth of practical information on how to overcome some of the difficulties of skin excoriation, sensitivity, etc.

The chapters on physiotherapy describe the pumping action of the leg muscles and the need to develop them to assist in draining the leg. Exercises, it is emphasized, form an important part of the treatment in addition to massage, posture, and leg elevation.

This book reveals no new and startling method of treatment of varicose veins, but rather re-emphasizes points which may have been forgotten, and coordinates all forms of conservative treatment into a very readable book.

The scope of the treatment should be well within the capabilities of most industrial medical departments. Those who undertake such treatment should read this book to remind themselves of the possibilities of a combined attack on the varicose vein problem.

R. A. TREVETHICK

Practical Allergy. By M. Colman Harris and Norman Shure. (Pp. xiii + 471; 25, figures 16 tables. 52*s*.6*d*.) London: Butterworths. 1958.

This book is an elementary account of practice in allergic aspects of medicine as carried out in the United States of America. It gives a superficial account of the nature of allergy and laboratory procedures in diagnosis. It gives various lists of allergens, many of which, particularly in relation to plants and animals, are irrelevant to British practice. There is throughout the book a tendency to assume that any condition is allergic unless proved otherwise which is not the approach to medicine usually recommended in British medical schools. In many respects the advice on clinical medicine is misleading. Emphysema is described as an allergic disease in which "the *x*-ray picture is diagnostic". It is difficult to imagine any statement further from the truth.

C. M. FLETCHER

Diagnostic Performance Tests. By Boris Semeonoff and Eric Trist; Forward by P. E. Vernon. (Pp. xv + 176; illustrated. 32*s*.) London: Tavistock Publications. 1958.

This manual describes test material, administration, scoring, tentative norms, qualitative interpretations and statistical data for the Semeonoff-Vigotsky, Trist-Hargreaves, Trist-Misselbrook-Kohs, Carl hollow square, and revised passalong tests. Appendices give intelligence test data and a full account of the Mitchell vocabulary test.

Flexible administration demands thorough knowledge of tests; qualitative interpretation requires an experimental and statistical approach to results. This book, providing the basis for both, will be valuable to all who use the tests.

SHEILA CHOWN

International Journal of Health Education. 1958. The International Union for Health Education of the Public was founded in 1951 and its assembly held in Rome in 1956 included 1,500 participants from 50 countries. It has now inaugurated a quarterly journal, of which this is the first issue, under the aegis of an editorial committee, of which Dr. John Burton, lately Director of the Central Council for Health Education, is a member.

Dr. M. G. Candau on behalf of W.H.O. and Professor Parisot (France), Honorary President of the sponsoring organization, have contributed messages of welcome.

The journal contains about a dozen short articles each of which has been written by an expert. All are well written and make easy and interesting reading. It is clearly impossible to refer to each of them individually and two only will be mentioned, as possibly these are of greatest interest to readers in this country.

The first deals with health education in industry and is written by Dr. Alfredo Bravo of Chile. Although very general in scope and in parts trite, it contains a lot of sound commonsense which, alas, is often lacking. The need to correlate health while at work with health in the home is emphasized. In the other, Dr. Betty Bond of Minneapolis describes an experiment to measure and compare the motivation resulting from lectures and discussion-decision group talks respectively, advocating preliminary examination by a physician followed by monthly self-examination of the breast as measures to secure the early diagnosis of cancer. The results come down heavily in favour of the discussion-decision group method.

A theme underlying many of the papers, and illustrated by a short story entitled "Once upon a time . . ." is that we should seek to discover the real needs of those we want to help.

The world-wide interest in this field is shown by articles on places as far apart as Canada, Central Africa, New Zealand, Japan, Yugoslavia and the U.S.S.R.

The greatest value of the journal will probably be to those who are planning or carrying out health education in those parts of the world where ignorance of health matters is more abysmal than in these islands. They should find much of the material instructive and may well find new and useful ideas which can be applied in other areas. They should also find encouragement in their often frustrating task of reading of the successes and even the failures of others.

A few notes towards the end of the issue are given regarding some new books, reports, films, and visual aids.

C. O. S. BLYTH BROOKE

BOOKS RECEIVED

(Review in a later issue is not precluded by notice here of books recently received.)

Statistics of Smoking. Tobacco Manufacturers' Standing Committee. Research Papers No. 1. Edited by G. F. Todd. (64 foolscap pages.) 1957.

Lavorazioni che espongono all'azione del **Cloruro di Carbonile (Fosgene).** By G. Giuliano and M. Rafanelli. (Pp. 58. Monograph.) Rome: Edizioni I.N.A.I.L. 1957.

Lavorazioni che espongono all'azione del **Cadmio-Leghe e Composti.** By G. Schippa and M. Rafanelli. (Pp. 72; 7 figures. Monograph.) Rome: Edizioni I.N.A.I.L. 1957.

IV Congreso Venezolano de Cirurgia, Vol. II, 17-21 March, 1957. (Pp. 577-1028; illustrated.) Caracas: Sociedad Venezolana de Cirurgia. 1957.

Proceedings of the XII International Congress on Occupational Health, Helsinki, 1-6 July, 1957, Vol. III (in English, French, and German). (Pp. 622; illustrated. Fin. marks 4,000.-.). Helsinki: Tyoterveyslaitos. 1957.

International Journal of Health Education. International Union for Health Education of the Public. 1958.

Grundlagen der Rehabilitation in der Bundesrepublik Deutschland. By K. A. Jochheim. (P. 203.) Stuttgart: Georg Thieme. 1958.

The Life and Work of Thomas Porter McMurray. By B. McFarland. (Pp. 12. 5*s*.) Liverpool University Press. 1958.

Digest of Pneumoconiosis Statistics 1956. Ministry of Fuel and Power. (Pp. 20. 3*s*.) London: H.M.S.O. 1958.

Here's to Good Health. A Collection of Articles on Health Subjects. By L. G. Norman; foreword by The Rt. Hon. Lord Evans. (Pp. 100.) London Transport Executive. 1958.

The Matrix of Medicine. By Nicolas Malleson. (Pp. xviii + 234. 45*s*.) London: Pitman Medical Publications. 1958.

The Nuffield Provincial Hospitals Trust. A record of the progress of schemes and descriptions of new projects 1955-1958. Fourth Report. (Pp. 70.) London: Nuffield Foundation. 1958.

The Determination of the ABO and Rh (D) Blood Groups for Transfusion. M.R.C. Memorandum No. 36 [revision of War Memorandum No. 9]. (Pp. 46. 3*s*. 6*d*.) London: H.M.S.O. 1958.

Ageing and Human Skill. By A. T. Welford. (Pp. viii + 300; illustrated. 25*s*.) Published for the Nuffield Foundation by Oxford University Press, London. 1958.

Tata Industrial Health Refresher Course 1957. (Pp. 22; illustrated.) Tata Industries. 1958.

Insecticide Resistance in Arthropods. By A. W. A. Brown. [W.H.O. Monograph Series No. 38.] (Pp. 240; 29 figures, 60 tables. 25*s*.) London: H.M.S.O.; Geneva: World Health Organization. 1958.

International Standards for Drinking-Water. (Pp. 152. 20*s*.) London: H.M.S.O.; Geneva: World Health Organization. 1958.

Handbook of British Occupational Hygiene Society. By C. N. Davies. (Pp. 39.) London: Pergamon Press. 1958.

Research Work Published in Sweden (Reprint).

Development of Lightning and Thunderstorm Research. By Harald Norinder. (Pp. 32). Stockholm: Almqvist & Wiksell. June, 1958.

Revolution in Medicine. By Brian Inglis. (Pp. 279. 21*s*.) London: Hutchinson. 1958.

Sonderausschuss Radioaktivität: First Report. (Pp. 68; 5 figures, 10 tables. DM 4.50.) Stuttgart: Georg Thieme. January, 1958.

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Joint FAO/WHO Expert Committee on Nutrition: Fifth Report [WHO Tech. Rep. Ser. No. 149]. (Pp. 55. 3*s*. 6*d*.) London: H.M. Stationery Office; Geneva: World Health Organization. 1958.

Mental Health Manual. By David Stafford-Clark; illustrated by Sylvia Treadgold. (Pp. 86; 16 figures.) London: British Red Cross Society. 1958.

The Healing Voice. By A. Philip Magonet. (Pp. viii + 205. 18*s*.) London: Heinemann. 1959.

13th International Congress on Occupational Health

The 13th international congress on occupational health will be held at the Waldorf Astoria Hotel, New York City, from July 25 to July 29, 1960. The Chairman of the Organizing Committee is Dr. Leo Wade, Medical Director, Esso Standard Oil Company, New York.

The programme will be devoted to the discussion of administrative, medical, and surgical practices; education and training; social and legal aspects; environmental hygiene; influence of environmental factors in health; work physiology and psychology; specific industries; general.

Those desiring to present papers must submit abstracts before January 1, 1960, to **Dr. Irving R. Tabershaw, Chairman of the Scientific Programme Committee, International Congress on Occupational Health, 375 Park Avenue, New York City.**

Abstracts should not contain more than 200 words, typed double-space. Original contributions rather than a review of previously published material will be given priority. Three copies in English are required and one copy in another official language of the Congress.

All abstracts will be reviewed by the Scientific Programme Committee. Selection will be based on the areas of interest as listed and the programme space allotted to each section. Authors will be notified before March 1, 1960, whether their papers have been accepted for presentation.

The names, academic degrees, titles, and complete addresses of author and co-author must be included in each abstract. The author who is to present the paper should be the first author listed in the abstract.

At the time the abstract is submitted the author must indicate that the paper will be presented at the Congress.

Complete texts of the papers in any one of the official languages of the Congress must be submitted not later than April 1, 1960.

The time allotted for each paper will be strictly limited to 15 minutes including slides.

The abstract will be published in the Proceedings which will be issued at the time of the Congress, and complete papers will be published later in the Proceedings of the Congress.

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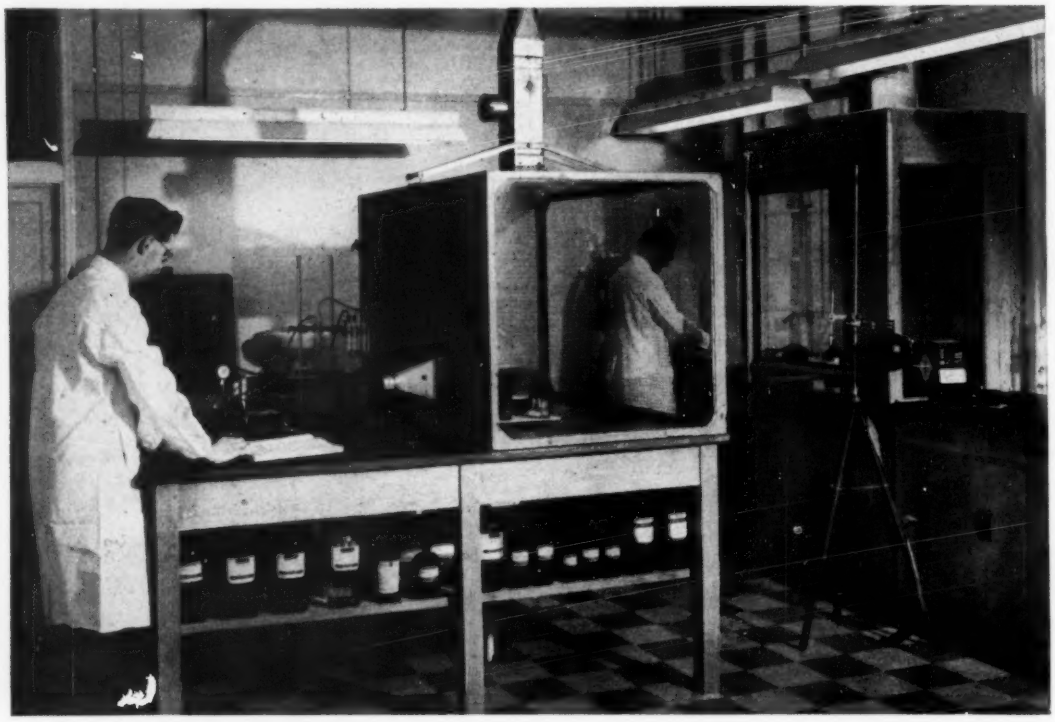

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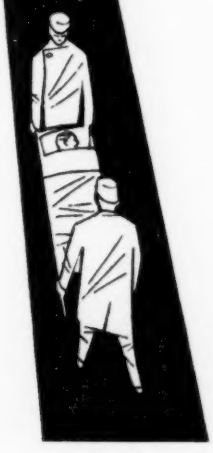

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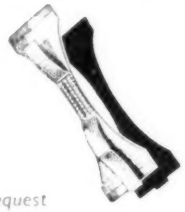

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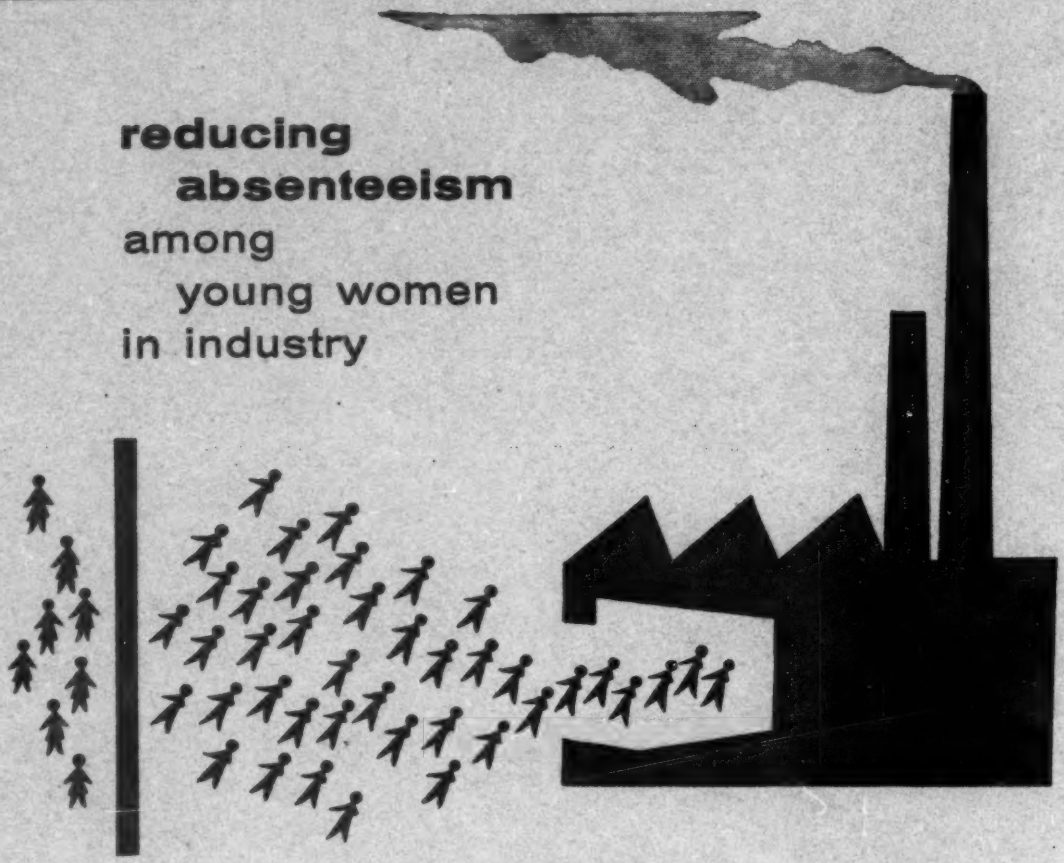

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